## JS AND COMPOSITIONS FOR INCREASING ANTIBODY PRODUCTION Attorney Docket P1957R1 Reilly et al.

Sheet 4 of 33

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## DS AND COMPOSITIONS FOR INCREASING ANTIBODY PRODUCTION Reilly et al. Attorney Docket P1957R1 Sheet 5 of 33

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# ANTIBODY PRODUCTION Reilly et al.

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FIG. 4D

ML. AODS AND COMPOSITIONS FOR INCREASING ANTIBODY PRODUCTION
Reilly et al. Attorney Docket P1957R1
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01 ECCTOSATGC TORREGERIR GOCTIGSTIA TGCCGGIRCT GCCGGGECTC TRECG GGGRCCTACG ACATCCGRAT CCGRACCAAT ACGGGEATGA CGGGCGGGG AACGC Inventor: REILLY ET AL. Docket No.: 11669.195USU1

itle: METHODS AND COMPOSITIONS FOR INCREASING ANTIBODY PRODUCTION

Serial No.: 10/697,995

GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GIJGATTGAT CAGGTAGAGG CTIGACACAC GOGICCAICI ICGAAACCIC IAAIAGCAGI GACGIIACGA AGCGIIAIAC CGCGIIIIAC IGGIIGICGC CAACIAACIA GICCAICICC 101

GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAAATC TCATTGCTGA GTTGTTATTT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT CITAAGIIGA AGAGGIAIGA AACCIAIICC IIIAIGICIG IACIIIIIAG AGIAACGACI CAACAAIAAA IICGAACGGG IIIIIICIICI ICICAGCIIA GGGCGCTGTA CGAGGTAAAG CCCGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TIGAAGCATC CTCGTCAGTA CCGCGACAT GCTCCATITC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TITCTICAAT AACTICGTAG GAGCAGICAI 201

AAAAGTTAAT CTTTTCAACA GCTGTCATAA AGTTGTCACG GCCGAGACTT ATAGTCGCTT TGTTTTTATT TTTTAATGTA TJTGTAACTA GTACGCAAGT ITTTCAATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA 301

TCACGIAAAA AGGGIATCIA GAATIAIGAA GAAGAATAIC GCATIICIIC IIGCAICIAI GIICGIIIII ICIAIIGCIA CAAACGCGIA CGCIGAIAIC AGTGCATITI TCCCATAGAT CITAATACIT CITCTTATAG CGTAAAGAAG AACGTAGATA CAAGCAAAAA AGATAACGAT GTITGCGCAT GCGACTATAG Anti-Tissue Factor Light Chain × « SIAT رب ح د X X AFLL Signal Sequence TIR-1 z × STII × 40.1

CGGAGACACC CGCTATCCCA GTGGTAGTGG ACGTCTCGGT CAGCGCTGTA GTTCTCGATA GACTTGACCA GCCTCTGTGG GCGATAGGGT CACCATCACC TGCAGAGCCA GTCGCGACAT CLÁGAGCTAT CTGAACTGGT œ A N T T ۵ ۷ > S 4 CICCCIGICC GAGGGACAGG S . CAGATGACCC AGTCCCCGAG TCAGGGGCTC œ GTCTACTGGG Σ 501 26

CGAGGCTTTC ATGACTAAAT GATACGATGA TCAGAGCGAC TTCCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCTG 601 ATCAACAGAA ACCAGGAAAA GCTCCGAAAG TACTGATTTA CTATGCTACT AGTCTCGCTG AAGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC œ S ი. > ე SLAE Y ۵. TGGTCCTTTT **IAGTIGICT** 0 9

TGTCCCATGG CGGTCTTCTG AAGCGTTGAA TAATGACAGA AGTCGTGCCT CTCAGAGGTA CCTGTAAACG GAGTCTCCAT GGACATTTGG ۵, ဟ TTCGCAACTT ATTACTGTCT TCAGCACGGA × ں. >-<u>۲</u> æ GCCAGAAGAC CTGACCATCA GCAGTCTGCA CCTAATGTGA GACTGGTAGT CGTCAGACGT u <u>ا</u> GGATTACACT 701 S

# FIG. 1A

Title: METHODS AND COMPOSITIONS FOR INCREASING ANTIBODY PRODUCTION

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CACACGGACG \_ ACGAAGACAA S TOTGGCTGCA CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TTAGACCTTG ပ S CTCGTCAACT J 0 வ CGGTAGACTA Ω S a. AGTAGAAGGG Œ, GGTAGACAGA S ACACCGACGT 4 æ > TCAAACGAAC AGTTTGCTTG ₩ • 801 AAGGTGGAGA TTCCACCTCT ω > × 126

GICACAGAGC AGGACAGCAA TCCTGTCGTT Ω CAGTGTCTCG ப ٢ GAGGCCAAAG TACAGTGGAA GGTGGATAAC GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GCCCATTGAG GGTCCTCTCA လ W 0 S z ပ CCACCTATTG CGGGAGGTTA 0 \_ æ z Ω > CICCGGTITC AIGICACCIT 3 0 × æ CTATCCCAGA GATAGGGTCT ۵. ACTIATIGAA TGAATAACTT z 901 160

TCACCCATCA GGGCCTGAGC AGTGGGTAGT CCCGGACTCG ပ 0 CANAGICIAC GCCIGCGAAG CGGACGCTTC w O GTTTCAGATG >-> × AAAGCAGACT ACGAGAACA TGCTCTTTGT × × ω TTTCGTCTGA Q 4 GACGCTGAGC CTGCGACTCG S ٦ GCAGCACCCT CGTCGTGGGA ٦ ٦ S TACAGCCTCA ATGTCGGAGT ဟ CCTGTCGTGG GGACAGCACC ₽ ഗ Ω 1001 193

CAACAGGGGA GAGTGTTAAT TAAATCCTCT ACGCCGGACG CATCGTGGCG AGCTCGGTAC CCGGGGATCT AGGCCTAACG CTCACAATTA ATTTAGGAGA TGCGGCCTGC GTAGCACCGC TCGAGCCATG GGCCCCTAGA TCCGGATTGC ပ w GTTGTCCCCT ပ œ z TCGCCCGTCA CAAAGAGCTT GTTTCTCGAA S AGCGGGCAGT > ഗ 1101 226

TIATCGICAC IGCAAIGCIN CTCGGTTGCC GCCGGCGTT TTTATTGTT GCCGACGCGC ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA GAGCCAACGG CGGCCCGCAA AAAATAACAA CGGCTGCGCG TAGAGCTTAC TTGACACACAC 1201

ACGTTACGAA

CGAAACCTCT AATAGCAGTG

CGTCCATCTT

CGCAATATGG CGCAAAATGA CCAACAGCGG TIGATTGATC AGGTAGAGGG GGCGCTGTAC GAGGTAAAGC CCGATGCCAG CATTCCTGAC GACGATACGG GCGTTATACC GCGTTTTACT GGTTGTCGCC AACTAACTAG TCCATCTCCC CCGCGACATG CTCCATTTCG GGCTACGGTC GTAAGGACTG CTGCTATGCC 1301

CGATTACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAAGTTAATC TTTTCAACAG CTGTCATAAA GTTGTCACGG CCGAGACTTA TTCTTCAATA ACTTCGTAGG AGCAGTCATT TTTCAATTAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT TCGACGACGC GCTAATGCAT AGCTGCTGCG 1401

ATCAGCGAAA CAAAAATAAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCATTTTT CCCATAGATC TTAATACTTC TTCTTATAGC GTAAAGAAGA 1501 TAGTCGCTTT GTTTTTATTT TITAATGTAT TIGTAACTAG TACGCAAGTT CACGTAAAAA GGGTATCTAG AATTATGAAG AAGAATATCG CATTTCTTCT X X Y Y L L ×

'STII Signal Sequence TIR-1

Inventor: REILLY ET AL. Docket No.: 11669.195USU1 Title: METHODS AND COMPOSITIONS FOR INCREASING ANTIBODY PRODUCTION

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GAGTGAGGCA CTCACTCCGI  $\alpha$ \_ AGCCAGGGG CGGTCCCC ပ a. GCCTGGTGC CCGGACCACG > \_ ပ Anti-Tissue Factor Heavy Chain GTCTGGCGGT CAGACCGCCA ပ S GCTGAGGTTC AGCTGGTGGA TCGACCACCT > ٦. CGACTCCAAG > w æ CTATTGCTAC AAACGCGTAC TTTGCGCATG >æ z GATAACGATG 4 TICGITITI AAGCAAAAAA S Ç., > TGCATCTATG ACGTAGATAC Σ ဟ ~ 1601 2

AACTAACTAG TIGATICATO ATGGGTTGGA TACCCAACCT GCCCCGGGTA AGGGCCTGGA TCCCGGACCT CGGGGCCCAT GGTCCGTCAG CCAGGCAGTC > ACATGCACTG TGTACGTGAC 3 AAGGAGTACT TTCCTCATGA >-GAAGTTATAA CTTCAATATT z (ب CAGCTTCTGG GTCGAAGACC ပ ഗ 4 TTGTCCTGTG AACAGGACAC O S 1701 3

G > . ပ ပ a. 0 α; × Σ W

ACTTGTCGGA TGAACAGCCT TACCTGCAGA ATGGACGTCT AAACACAGCA TTTGTGTCGT ACAATTCCAA TGTTAAGGTT TATTCGCGAC ATAAGCGCTG GCCACGGTGA CCGTGCCACT AGTICCAGGA TCAAGGTCCT TATGACCCGA ATACTGGGCT CAACACGATC GTTGTGCTAG CAGAGCAAGG GTCTCGTTCC ပ w 1801 77

GAGCCGGAGG CTCGGCCTCC S z TCACCGTCTC AGTGGCAGAG 0 GGAACCCTGG CCTTGGGACC æ **(-**z CTGGGGTCAA GACCCCAGTT × တ z ACTICGACTA TGAAGCTGAT ~ S TGCCGGCGAA ACGGCCGCTT €-4 œ ACGAGCTCTG TGCTCGAGAC Ω 0 ĹL. TCTATTATTG AGATAATAAC o. 0 >-CTGTGACGC GACACTGCCG ← z GCGTGCTGAG CGCACGACTC 0 1901

AAGGGGCTTG TTCCCCGAAC CAAGGACTAC GTTCCTGATG CGACGGACCA GCTGCCTGGT CGCCGGGACC GCGGCCCTGG TGGGGGCACA ACCCCCGTGT CCCTCCTCCA AGAGCACCTC TCTCGTGGAG GGGAGGAGGT CCCCCTGGCA GGGGGACCGT CATCGGTCTT GTAGCCAGAA > ACCAAGGGCC TGGTTCCCGG ပ × 2001 143

പ 0 \_ O \_ 4 ပ ပ S  $\leftarrow$ ഗ S S 4 \_ ۵, S

GCAGCGTGGT CGTCGCACCA > S TACTCCCTCA ATGAGGGAGT \_ S GAGTCCTGAG CTCAGGACTC ... ပ S TCCTACAGTC AGGATGTCAG S 0 \_ AAGGGCCGAC TTCCCGGCTG 4 ۵. GCACGTGTGG CGTGCACACC • = > TGACCAGCGG ACTGGTCGCC ပ ഗ €⊸ TCAGGGGCCC AGTCCGCGGG \_ æ ပ GTCGTGGAAC CAGCACCTTG z 3 S CGGTGACGGT GCCACTGCCA 2101 177

CGGGTTTAGA GCCCAAATCT × ൨ AGAAAGTTGA TETTTCAACT > AAGGTGGACA TTCCACCTGT Ω > × CAGCAACACC GTCGTTGTGG €-z ഗ TGCAACGTGA ATCACAAGCC TAGTGTTCGG  $\mathbf{x}$ × ACGITGCACT > z TGGGCACCCA GACCTACATC CTGGATGTAG >-٤¬ ACCCGTGGGT O ٢ ပ TCTAGCAGCT AGATCGTCGA S ഗ GACTGTGCCC CTGACACGGG ۵, >  $\leftarrow$ 2201 210

ACCCTCATGA .. TCCCCCAAA ACCCAAGGAC TGGGTTCCTG × AGGGGGTTT Ω, ۵. GTCTTCCTCT CAGAAGGAGA L [e, > GGGACCGTCA CCCTGGCAGT ഗ വ ഗ TTGAGGACCC **AACTCCTGGG** ပ **د.** CCAGCACCTG GGTCGTGGAC ω Ω. æ CCCACCGTGC GGGTGGCACG O م Ω, CTCACACATG GAGTGTGTAC =TGTGACAAAA ACACTGTTT Ω 2301 243

Inventor: REILLY ET AL.
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AGGTGCATAA TCCACGTATT × > GACGCCCTGG CTGCCGCACC > ပ CTGGTACGTG GACCATGCAC > > 3 TCAAGTTCAA AGTTCAAGTT z Ç, × CTGGGACTCC GACCCTGAGG (L) ۵, GAGCCACGAA CTCGGTGCTT Œ × S TGGTGGACGT ACCACCTGCA Ω > CCCTGAGGTC ACATGCGTGG TGTACGCACC > > ပ GGGACTCCAG > w ρ, TCTCCCGGAC AGAGGGCCTG œ 2401 277

CAAGGAGTAC GTTCCTCATG w GCCTGAATGG CCGACTTACC G z د. GTGGTCCTGA CACCGTCCTG CACCAGGACT Ω 0 = GTGGCAGGAC \_ > €--AGTCCCAGGA TCAGCGTCCT > ഗ TACCGTGTGG ATGGCACACC > œ GTTGTCGTGC TGCCAAGACA AAGCCGCGGG AGGAGCAGTA CAACAGCACG ۲ S z TCCTCGTCAT 0 ω TTCGCCCCC £ œ ۵. × ACGGTTCTGT 2501 310

ACCCTGCCCC TGGGACGGG ۵. <del>ب</del> ACAGGTGTAC TGTCCACATG > CCCGAGAACC GGCTCTTGG cu œ AAAGGGCAGC TTTCCCGTCG 0 ပ GAGGTTTCGG CTCCAAAGCC æ × S TCTTTTGGTA AGAAAACCAT ٤-× GCCCCCATCG CGGGGGTAGC ω -A . AGCCCTCCCA TCGGGAGGGT ۵. ... ~ TCTCCAACAA AGAGGTTGTT z ഗ AAGTGCAAGG TTCACGTTCC × U يد 2601

GCAATGGGCA CGTTACCCGT 0 ပ z GAGTGGGAGA CTCACCCTCT L 3 CATCGCCGTG GTAGCGGCAC > ~ ATCCCAGCGA TAGGGTCGCT Ω တ م AAAGGCTTCT TTTCCGAAGA Œ. ပ TCAGCCTGAC CTGCCTGGTC GACGGACCAG > ... ں AGTCGGACTG \_ တ AAGAACCAGG TTCTTGGTCC 0 z AGAGATGACC TCTCTACTGG Σ ω CATCCCGGGA GTAGGGCCCT æ S 2701

GTGGCAGCAG CACCGTCGTC 0 3 ACAAGAGCAG TGTTCTCGTC ഗ CTCACCGTGG GAGTGGCACC > **-**CTACAGCAAG GATGTCGTTC × S >-CCTTCTTCCT GGAAGAAGGA \_ Cı. Œ. AGGCTGCCGA TCCGACGGCT ပ Ω GCACGACCTG CGTGCTGGAC 0 . . CCACGCCTCC GGTGCGGAGG Ω, ۵. ۲ AACTACAAGA TTGATGTTCT × >-GCCGGAGAAC CGCCTCTTG z ធ ۵. 2801 410

TAMATAMECA TECENCECC ATTTATTCGT TGTCTCCGG ACAGAGGCCC ۵, S AGCCTCTCCC TCGGAGAGGG S ... GAGGCTCTGC ACAACCACTA CACGCAGAAG GTGCGTCTTC × 0 TGTTGGTGAT >-= z CTCCGAGACG \_ æ CGTGATGCAT GCACTACGTA  $\equiv$ Σ > TCTCATGCTC AGAGTACGAG ഗ ပ S CCCTTGCAGA GGGAACGTCT > z O 2901

TTTATCACAG AATAGTGTC AATGCGGTAG CGCAAAAAAT AACAATTGAG TACAAACTGT CGAATAGTAG CTATTCGAAA TTACGCCATC GATAAGCTTT GCTTATCATC TIGITAACIC AIGITIGACA GCGTTTTTTA TTGCCGCCGG ATTGCGAGCC AACGGCGGCC TAACGCTCGG SATCTCAGGG CTAGAGICCC 3001

ATAGGCTTGG TATCCGAACC TGCTGTAGGC AGTGGGACCT AGGACATCCG TCACCCTGGA CATCGTCATC CTCGGCACCG GTAGCAGTAG GAGCCGTGGC ACAATGCGCT TGTTACGCGA ATGAMATCTA TACTTTAGAT GGCACCGTGT CCGTGGCACA AACGCAGTCA TTGCGTCAGT TTANATIGCT AATTTAACGA 3101

Start Tet Resistance Coding Sequence

CTATATGCGT TGATGCAATT CGACGATCGC GATATACGCA ACTACGTTAA GCTGCTAGCG ATCCCCAGTC ACTATGGCGT TAGCGGTCAG TGATACCGCA TTCCGACAGC AAGGCTGTCG ATATCGTCCA TGACGCCCC GAGAACGCCC TATAGCAGGT CTCTTGCGGG ACTGCCGGGC TTATGCCGGT AATACGGCCA 3201

# FIG. 1D

Inventor: REILLY ET AL. Docket No.: 11669.195USU1

Title: METHODS AND COMPOSITIONS FOR INCREASING ANTIBODY PRODUCTION

Serial No.: 10/697.

INGGATAAGG AAATACAGAC ATGAAAAATC TCATTGCTGA GTTGTTATTT AAGCTTGCCC AAAAGAAGA AGAGTCGAAT CAGGTAGAGG TCGADACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC CGCGTTTTAC TGGTTGTCGC CAACTAACTA GTCCATCTCC GTTGATTGAT AGAGGTATGA AACCTATTCC TITATGTCTG TACTITITAG AGTAACGACT CAACAATAAA TICGAACGGG TITTTCTTCT ACCAACAGCG GCGCAAAATG TCGCAATATG CTGCAATGCT ATTATCGTCA AGCTTTGGAG TCTCCATACT CGCAGGTAGA GCGTCCATCT GAATTCAACT CTTGACACAC CITAAGIIGA GAACTGTGTG 101

CTCGTCAGTA CICGACGACG CGCIAAIGCA ITICITCAAI AACITICGIAG GAGCAGICAI TTGAAGCATC CGAGGTAAAG CCCGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA GGGCTACGGT CGTAAGGACT GCTGCTATGC GCTCCATTTC GGCGCTGTA CCCGCGACAT 201

ITITCAATTA GAAAAGITIGI CGACAGIAIT ICAACAGIGC CGGCICIGAA TAICAGCGAA ACAAAAAIAA AAAAITACAI AAACAÍIGAI CAIGCGITCA 301 AAAAGTTAAT CTTTTCAACA GCTGTCATAA AGTTGTCACG GCCGAGACTT ATAGTCGCTT TGTTTTAAT TTTTAATGTA TTTGTAACTA GTACGCAAGT

agtgcatitt teccatagat ettaataett ettittgtag egaaaagaag aaegtagata eaageaaaaa agataaegat gittgègeat gegaetatag TCACGTAAAA AGGGTATCTA GAATTATGAA GAAAACATC GCTTTTCTTC TTGCATCTAT GTTCGTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC start light chain (z, بع ح Σ တ Ø .1 \*start STII signal TIR-2 401

GIGGIAGIGG ACGICICGGI CAGCGCIGIA GITCIÓGAIA GACTIGACCA CTCCCTGTCC GCCTCTGTGG GCGATAGGGT CACCATCACC TGCAGAGCCA GTCGCGACAT CAAGAGCTAT CTGAACTGGT × Ω œ æ œ ۲  $\vdash$ ₽ CGGAGACACC CGCTATCCCA œ Ω ഗ GAGGGACAGG ഗ .7 S 501 CAGATGACCC AGTCCCCGAG TCAGGGGCTC Ω, S GTCTACTGGG ⋳ Σ o 26

ATCAACAGAA ACCAGGAAAA GCTCCGAAAG TACTGATTTA CTATGCTACT AGTCTCGCTG AAGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC CGAGGCTTTC ATGACTAAAT GATACGATGA TCAGAGCGAC TTCCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG ပ ∝ S ۵ ک SLA YAY 1 1 × d K TGGTCCTTTT ပ ۵, TAGTIGICTI 601 9

GGATTACACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTCT TCAGCACGGA GAGTCTCCAT GGACATTGG ACAGGGTACC ග o CGGTCTTCTG AAGCGTTGAA TAATGACAGA AGTCGTGCCT CTCAGAGGTA CCTGTAAACC ۵, တ Ö × o n u × FATY <u>а</u> Δ, CGTCAGACGT S GACTGGTAGT T T CCTAATGTGA 701 93

GIGICCICC AGTITIGCITIG ACACCGACGT GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA CACACGGACG TGCTTCTGTT <u>></u> æ TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC ပ တ ۲. ۳ o Ω ഗ E E CCATCTGTCT တ TGTGGCTGCA 4 > TCAAACGAAC TICCACCICI AAGGTGGAGA ធា > × 801 126

FIG. 2A

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CCAGGAGAGT GTCACAGAGC AGGACAGCAA CAGIGICICG ICCIGICGII GGTCCTCTCA Œ o CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC GCCCTCCAAT CGGGTAACTC CGGGAGGTTA GCCCATTGAG z ပ O CCACCTATTG Ω > CICCGGIITC AIGICACCIT 3 o Ø GATAGGGTCT Ω, TGAATAACTT ACTTATTGAA z 901 160

CAAAGTCTAC GCCTGCGAAG TCACCCATCA GGGCCTGAGC CCCGGACTCG ဗ AGTGGGTAGT CGGACGCTTC Œ O æ GTTTCAGATG > > × GACGCTGAGC AAAGCAGACT ACGAGAAACA TGCTCTTTGT I × ω TTTCGTCTGA Ω æ × CTGCGACTCG တ ... TACAGCCTCA GCAGCACCCT CGTCGTGGGA H ₽ ഗ ATGTCGGAGT u ഗ GGACAGCACC CCTGTCGTGG ₽ တ Ω 1001 193

TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTTAAT TAAATCCTCT ACGCCGGACG CATCGTGGCG AGCTCGGTAC CCGGGGATCT AGGCCTAACG CTCACAATTA ATTTAGGAGA TGCGGCCTGC GTAGCACCGC TCGAGCCATG GGCCCCTAGA TCCGGATTGC 0 ပ ω GTTTCTCGAA GTTGTCCCCT G æ z ഗ × AGCGGGCAGT > တ 1101 226

CTCGGTTGCC GCCGGCGTT TTTATTGTT GCCGACGCGC ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGCAATGCTT BAGCCAACGG CGGCCCGCAA AAATAACAA CGGCTGCGCG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTTACGAA 1201

CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGGG GGCGCTGTAC GAGGTAAAGC CCGATGCCAG CATTCCTGAC GACGATACGG CTCCATITICG GGCTACGGIC GIAAGGACIG CIGCIAIGCC CCGCGACATG TCCATCTCCC GGTTGTCGCC AACTAACTAG GCGTTTTACT CGCAATATGG SCGTTATACC 1301

AGCTGCTGCG CGATTACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAAGTTAATC TTTTCAACAG CTGTCATAAA GTTGTCACGG CCGAGACTTA ICGACGACGC GCTAATGCAT TTCTTCAATA ACTTCGTAGG AGCAGTCATT TTTCAATTAG AAAAGTTGTC GACAGTATTT CAACÁGTGCC GGCTCTGAAT 1401

GAAAAGAAGA GGGTATCTAG AATTATGAAG AAAACATCG CTTTTCTTCT L Çe, TTTTGTAGC CCCATAGATC TTAATACTTC × TITAAIGIAI IIGIAACIAG IACGCAAGII CACGIAAAA ATCAGGGADA CAAAATAAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCATTTTT 1501 TAGTCGCTTT GTTTTTTTT

STII signal start :

GAGTGAGGCA \_ GCCTGGTGC AGCCAGGGGG cccaccacc rcccrcccc 0 > u GTCTGGCGGT CAGACCGCCA G ပ က 1601 TGCATCTATG TTCGTTTTTT CTATTGCTAC AAACGCGTAC GCTGAGGTTC AGCTGGTGGA ACGTAGATAC AAGCAAAAAA GATAACGATG TTTGCGCATG CGACTCCAAG TCGACCACCT start heavy chain L V E о > з Ø æ z æ > Æ,

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AACTAACTAG TTGATTGATC TGAACAGCCT ATGGGTTGGA TACCTGCAGA TACCCAACCT Ö 2 3 GCCCCGGGTA AGGGCCTGGA TCCCGGACCT AAACACAGCA Ĺ J G CGGGGCCCAT ACAATTCCAA  $\simeq$ Ö ۵, æ GGTCCGTCAG ATAAGCGCTG CCAGGCAGTC O œ > CITCAAIAIT AAGGAGIACI ACAIGCACIG CCGTGCCACT TGTACGTGAC 3 x Σ TTCCTCATGA AGTTCCAGGA > ш TATGACCCGA GAAGTTATAA z Œ, CAGCTTCTGG CAACACGATC GTCGAAGACC ပ ഗ æ Trercerere AACAGGACAC CAGAGCAAGG O ഗ -1701 1801 43

ACTIGICGGA L ഗ z ATGGACGTCT O TTTGTGTCGT 4 ₽ z TGTTAAGGTT × ഗ Z TATTCGCGAC Ω A လ GGCACGGTGA H æ 04 TCAAGGTCCT Ω O (L, ATACTGGGCT ۵, Ω GTTGTGCTAG E z GTCTCGTTCC Ö 0 W 77

CTCGGCCTCC GAGCCGGAGG ഗ ഗ TCACCGTCTC AGTGGCAGAG ₽ GGAACCCTGG CCTTGGGACC L ₽ O TGCTCGAGAC ACGCCGCTT ACTTCGACTA CTGGGGTCAA GACCCCAGTT 0 G 3 TGAAGCTGAT  $\rightarrow$ Ω ſz, TGCCGGCGAA æ A ₽ ACGAGCTCTG Ω œ 4 TCTATTATTG AGATAATAAC C >->-GACACTGCCG CTGTGACGGC æ ₽ GCGTGCTGAG CGCACGACTC ω K œ 1901 110

TTCCCCGAAC AAGGGGCTTG Ω, GTTCCTGATG CAAGGACTAC > × CGACGGACCA GCTGCCTGGT .\_ O GCGCCCTGG CGCCGGGACC J æ TGGGGGCACA ACCCCCGTGT E Ö Ö TCTCGTGGAG CCCTCCTCCA AGAGCACCTC ₽ တ GGGAGGAGGT × S ഗ ρ, CCCCCTGGCA GGGGGACCGT æ u Ω. GTAGCCAGAA CATCGGTCTT > S ACCAAGGGCC TGGTTCCCGG G ₽ 2001 143

CGTCGCACCA GCAGCGTGGT > ഗ TACTCCCTCA ATGAGGGAGT S .. S GAGTCCTGAG CTCAGGACTC H ဗ တ AAGGGCCGAC AGGATGTCAG TCCTACAGTC လ O H Trecegere K ۵, CGTGCACACC GCACGTGTGG E  $\Xi$ > TGACCAGCGG ACTGGTCGCC G တ GTCGTGGAAC TCAGGCGCCC AGTCCGCGGG H æ Ö S CAGCACCTTG z 3 တ CGGTGACGGT GCCACTGCCA > 2101 177

CGGGTTTAGA GCCCANATCI ഗ × <u>م</u> AAGGTGGACA AGAAAGTTGA TCTTTCAACT (L) × TTCCACCTGT Ω > CAGCAACACC GTCGTTGTGG E Ż ഗ TGCAACGTGA ATCACAAGCC TAGTGTTCGG × =ACGITGCACT > Z GACCTACATC CTGGATGTAG > ₽ TGGCCACCCA ACCCGTGGGT O ₽ G TCTAGCAGCT AGATCGTCGA S တ CTGACACGGG GACTGTGCCC ۵. > ₽ 2201 210

ACCCTCATGA TGGGAGTACT H GICTICCICI ICCCCCAAA ACCCAAGGAC TGGGTTCCTG ρ. AGGGGGGTTT ρ, ρ, CAGAAGGAGA Œ, H ÇE, > GGGACCGTCA CCCTGGCAGT S ρ, Ö CCAGCACCTG AACTCCTGGG TTGAGGACCC Ö L L GGTCGTGGAC ρ, æ Ω, CCCACCGTGC GGGTGGCACG C Δ, Ω, CTCACACATG GAGTGTGTAC O H = TGTGACAAAA ACACTGTTTT 2301 243

GACGGCGTGG AGGTGCATAA TCCACGTATT × CTGCCGCACC Ö Ω CTGGTACGTG GACCATGCAC > 3 TCAAGTTCAA AGTTCAAGTT Ĺ. GAGCCACGAA GACCCTGAGG CTGGGACTCC > ш ۵, CTCGGTGCTT = လ ACATGCGTGG TGGTGGACGT ACCACCTGCA Ω TGTACGCACC > O CCCTGAGGTC GGGACTCCAG > ω ۵, TCTCCCGGAC AGAGGCCTG œ တ 2401 277

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GTTCCTCATG TGCCAAGACA AAGCCGCGGG AGGAGCAGTA CAACAGCACG TACCGTGTGG TCAGCGTCCT CACCGTCCTG CACCAGGACT GGCTGAATGG CAAGGAGTAC CCGACTTACC z GTGGCAGGAC GTGGTCCTGA Ω o H GTTGTCGTGC ATGGCACACC AGTCGCAGGA > α. ഗ z TCCTCGTCAT > O (L) Tregeeecc œ Ω, ACGGTTCTGT 2501 310

TGGGACGGG CCCGAGAACC ACAGGTGTAC ACCCTGCCCC ۵, TGTCCACATG GGCTCTTGG ш œ AGCCCTCCCA GCCCCCATCG AGNAAACCAT CTCCAAAGCC AAAGGGCAGC TTTCCCGTCG O ပ GAGGTTTCGG × ഗ TCTTTTGGTA CGGGGGTAGC ۵, Ø TCGGGAGGGT L K AAGTGCAAGG TCTCCAACAA AGAGGTTGTT z TTCACGTTCC 2601 343

GCAATGGGCA CGTTACCCGT ပ CATCGCCGTG GAGTGGGAGA CTCACCCTCT ы ω GTAGCGGCAC > æ ù AAAGGCTTCT ATCCCAGCGA TITCCGAAGA TAGGGICGCT Ω S Ω, Ç., ဗ CTGCCTGGTC GACGGACCAG > L O AAGAACCAGG TCAGCCTGAC TCTCTACTGG TTCTTGGTCC AGTCGGACTG ₽ u S 0 z AGAGATGACC Σ (L) CATCCCGGGA GTAGGGCCCT 2701 377

GTGGCAGCAG CACCGICGIC 3 CTCACCGTGG ACAAGAGCAG rerrerect œ တ GAGTGGCACC > E CTACAGCAAG GATGTCGTTC × S > CCTTCTTCCT GGAAGAAGGA Çe, Çe, TCCGACGGCT AGGCTGCCGA ပ Ω ഗ GCACGACCTG CGTGCTGGAC GGTGCGGAGG CCACGCCTCC Δ, ρ, H AACTACAAGA TTGATGTTCT × >-GCCGGAGAAC CGCCTCTTG ш ۵, 2801 410

TGCGACGGCC TAAATAAGCA ATTTATTCGT TGTCTCCGGG ACAGAGGCCC CGTGATGCAT GAGGCTCTGC ACAACCACTA CACGCAGAAG AGCCTCTCCC TCGGAGAGGG တ L GTGCGTCTTC O <del>[-</del>4 TGTTGGTGAT = z CTCCGAGACG æ GCACTACGTA =Σ > TCTCATGCTC AGAGTACGAG U ഗ GGGAACGTCT CCCTTGCAGA > z ပ 2901 443

AATGCGGTAG TTTATCACAG ATTGCGAGCC AACGGCGGCC CGCAAAAAT AACAATTGAG TACAAACTGT CGAATAGTAG CTATTCGAAA TTAGGCCATC AAATAGTGTC TAACGCTCGG TTGCCGCCGG GCGTTTTTTA TTGTTAACTC ATGTTTGACA GCTTATCATC GATAAGCTTT SATCTCAGGG CTAGAGTCCC 3001

TIMANTIGCT AACGCAGTCA GCCACCGTGT ATGAAATCTA ACAATGCGCT CATCGTCATC CTCGGCACCG TCACCCTGGA TGCTGTAGGC ATAGGCTTGG ACGACATCCG TATCCGAACC GIAGCAGIAG GAGCCGIGGC AGIGGGACCI CCGTGGCACA TACTTTAGAT TGTTACGCGA TTGCGTCAGT AATTTAACGA 3101

\$ ACTGCCGGGC CTCTTGCGGG ATATCGTCCA TGACGCCCG GAGAACGCCC TATAGCAGGT TTATGCCGGT 3201

Docket No.: 11669.195USUI Title: METHODS AND COMPOSITIONS FOR INCREASING ANTIBODY PRODUCTION

TCATTGCTGA GITGITATIT AAGCITGCCC AAAAAGAAGA AGAGICGAAI GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG TCGAAACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC CGCGTTTTAC TGGTTGTCGC CAACTAACTA GTCCATCTCC CTCGTCAGTA CCGGGGACAT GCTCCATITC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TITCTICAAT AACTICGTAG GAGCAGTCAT CCCTGATATC GCGACTATAG TITTAATGTA TITGTAACTA GTACGCAAGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA Ω Anti-VEGF Light chain TTGAAGCATC TCTATTGCTA CAAACGCGTA CITAAGIIGA AGAGGIAIGA AACCIAIICC IIIAIGICIG IACIIIIIAG AGIAACGACI CAACAAIAAA IICGAACGGG IÏIIICIICI GTTTGCGCAT CGAGGTAAAG CCCGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA CAAGCAAAA AGATAACGAT SIAT TGTTTTTATT GTTCGTTTTT Œ. > ÇL, ATAGTCGCTT AACGTAGATA TTGCATCTAT Σ ဟ TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAAATC AAAAGTTAAT CTTTTCAACA GCTGTCATAA AGTTGTCACG GCCGAGACTT CGTAAAGAAG GCATTTCTTC £L. æ Signal TIR -1 GAAGAATATC CTTCTTATAG z STII GAATTATGAA CTTAATACTT × GCGTCCATCT AGGGTATCTA ITTICAATTA GAAAAGITGI TCCCATAGAT CTTGACACAC GGCGCTGTA TCACGTAAAA GAATTCAACT 301 101 201 401

ATCGTTGATA AATTTGACCA CACCATCACC TGCAGCGCAA GTCAGGATAT TAGCAACTAT TTAAACTGGT z z CAGTCCTATA Ω 0 ACGTCGCGTT 4 S GTGGTAGTGG CTCCCTGTCC GCCTCTGTGG GCGATAGGGT CGCTATCCCA œ 0 CGGAGACACC ပ > S ~ GAGGGACAGG S ... ഗ CAGITGACCC AGICCCCGAG TCAGGGGCTC S တ GTCAACTGGG 0 501

CAAGACCCTG TOTGGATCCG AGACCTAGGC S ပ AAGAGCGAAG TTCTCGCTTC ſ. œ ဟ GACCTCAGGG CTGGAGTCCC ۵. > ပ TCTCTCCACT AGAGGGGTGA × **ب** GAAGTGGAGG CTTCACCTCC ဟ €--Ĺ. CGAGGCTTTC ATGACTAAAT GCTCCGAAAG TACTGATTTA >-H J × Ω, æ ACCAGGAAAA TGGTCCTTTT × G Q, ATCAACAGAA TAGTTGTCTT 0 O 601 9

ACAGGGTACC ပ o GGACGTTTGG CCTGCAAACC TGTCATATCG TGGCACGGCA ACCGTGCCGT ۵, > L ATTACTGTCA ACAGTATAGC ഗ >-0 TAATGACAGT ပ >-AAGCGTTGAA TICGCAACTI Æ u CGGTCTTCTG GCCAGAAGAC Ω W GCAGTCTGCA CGTCAGACGT ۔. S CTGACCATCA GACTGGTAGT  $\vdash$ GGATTTCACT CCTAAAGTGA 701 3

recricter ererected ACGAAGACAA CACACGGACG CTCGTCAACT TTAGACCTTG AAGGIGGAGA ICAAACGAAC IGIGGCIGCA CCAICIGICI ICAICIICCC GCCAICIGAI GAGCAGIIGA AAICIGGAAC ပ 0 CGGTAGACTA ဟ GGTAGACAGA AGTAGAAGGG (L) ACACCGACGT æ TICCACCICT AGITIGCTIG œ 801 126

Inventor: REILLY ET AL.
Docket No.: 11669.195USU1
Title: METHODS AND COMPOSITIONS FOR INCREASING ANTIBODY PRODUCTION
Serial No.: 10/697,995

GTCACAGAGC AGGACAGCAA TCCTGTCGTT 0 CAGTGTCTCG H GCCCTCCAAT CGGGTAACTC CCAGGAGAGT CGGGAGGTTA GCCCATTGAG GGTCCTCTCA တ W 0 ഗ z ပ 0 J A CCACCTATTG CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC z ۵ > ATGTCACCTT 3 o CTCCGGTTTC > E A GATAGGGTCT 04 ۵, >-TGAATAACTT ACTTATTGAA ſ. z z 901 160

TCACCCATCA GGGCCTGAGC CCCGGACTCG AGTGGGTAGT =  $\leftarrow$ ACGAGAAACA CAAAGTCTAC GCCTGCGAAG GTTTCAGATG CGGACGCTTC > \( \omega O A **≻** > × TGCTCTTTGT =× ш GGACAGCACC TACAGCCTCA GCAGCACCCT GACGCTGAGC AAAGCAGACT TITCGICTGA ۲ ۵ **∢** ⊻ CTGCGACTCG S ٠. د CGTCGTGGGA H S CCIGICGIGG AIGICGGAGI ഗ s ≻  $\leftarrow$ 1001 193

TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTTAAT TAAATCCTCT ACGCCGGACG CATCGTGGCG AGCTCGGTAC CCGGGGGATCT AGGCCTAACG CTCACAATTA ATTTAGGAGA TGCGGCCTGC GTAGCACCGC TCGAGCCATG GGCCCCTAGA TCCGGATTGC ပ မ GTTGTCCCCT ပ œ z GTTTCTCGAA ഗ AGCGGCCAGT ρ, 1101 226

SAGCCAACGG CGGCCCGCAA AAAATAACAA CGGCTGCGCG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTTACGAA CTCGGTTGCC GCCGGCGTT TTTATTGTT GCCGACGCGC ATCTCGAATG AACTGTGTG GCAGGTAGAA GCTTTGGAGA TATCGTCAC TGCAATGCTT 1201

CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGGG GGCGCTGTAC GAGGTAAAGC CCGATGCCAG CATTCCTGAC GACGATACGG CICCATTICG GGCTACGGIC GAAAGGACIG CIGCIAIGCC GGTTGTCGCC AACTAACTAG TCCATCTCCC CCGCGACATG GCGTTTTACT CCCAATATGG SCGTTATACC 1301

AGCTGCTGCG CGATTACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAAGTTAATC TTTTCAACAG CTGTCATAAA GTTGTCACGG CCGAGACTTA CGACGACGC GCTAATGCAT TICTICAATA ACTICGIAGG AGCAGICATI TITCAATIAG AAAAGTIGIC GACAGIATIT CAACAGIGCC GGCTCTGAAT 1401

ATCAGCGAAA CAAAAATAAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCATTTTT CCCATAGATC TTAATACTTC TTCTTATAGC GTAAAGAAGA 1501 TAGTCGCTTT GITITIATIT ITIAATGTAT ITGTAACTAG TACGCAAGTI CACGTAAAAA GGGTATCTAG AAITAIGAAG AAGAATATCG CAITICTTCI

STII Signal TIR-1

ACGIAGAIAC AAGCAAAAA GAIAACGAIG ITIGCGCAIG CGACICCAAG ICGACCACCI CAGACCGCCA CCGGACCACG ICGGICCCCC GAGIGAGGCA 1601 TGCATCTATG TICGITITIT CIATIGCTAC AAACGCGTAC GCIGAGGITC AGCIGGIGGA GICIGGCGGI GGCCIGGIGC AGCCAGGGGG CICACICCGI o > .ე ც ပ L < E Anti-VEGF Heavy Chain ο > ω a z A Ca. > ဟ æ 2

FIG. 3B

Inventor: REILLY ET AL.
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Title: METHODS AND COMPOSITIONS FOR INCREASING ANTIBODY PRODUCTION

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TGGATTAACA ACCTAATIGI ATGGGTTGGA TACCCAACCT ပ > 3 GGTCCGTCAG GCCCCGGGTA AGGGCCTGGA CGGGGCCCAT TCCCGGACCT ω ۔۔ ပ ပ ۵. CCAGGCAGTC 0 œ > CTACGACTIC ACGCACTACG GTATGAACTG CATACTTGAC z Z GATGCTGAAG TGCGTGATGC ပ x €-G. Δ >-TTGTCCTGTG CAGCTTCTGG GTCGAAGACC S AACAGGACAC ပ

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TGAACAGCCT ACTTGTCGGA \_ ഗ Z. TACCTGCAGA ATGGACGTCT 0 \_ AAGCACAGCA Tregreres  $\vdash$ ഗ ACACCTCCAA TGTGGAGGTT × ഗ TTTTCTTTAG AAAAGAAATC Ω د. ဟ AGCAAAGTGA TCGTTTCACT -Œ. ∞. TATGCTGCGG ATTTCAAACG TANAGITIGG × G. ATACGACGCC Ω 4 ¥ X ACTIGGCTGG TGAACCGACC  $\vdash$ Ω, w CCTATACCGG GGATATGGCC ပ ٢ 1801 7

AACCCTGGTC TTGGGACCAG GGGGTCAAGG CCCAGTTCC ပ 0 G CCGTACTATT ACGCCACGAG CCACTGGTAT TTCGACGTCT AAGCTGCAGA > Ω GGTGACCATA >-3 × TGCCGTGCTC H ပ GGCATGATAA >->-GACACTGCCG TCTATTACTG TGCAAAGTAC ACGITICATG >-× K AGATAATGAC C >->-CTGTGACGGC æ H Ω GCCCCCTGAG CGCGCGACTC W ø. 1901 110

TGCCTGGTCA ACGGACCAGT \_ CCGGGACCCG GCCCTGGGC ပ ... GGGCCACAGC cccccrcrcc ~ €-ပ AGCACCTCTG TCGTGGAGAC ပ S F CTCCTCCAAG GAGGAGGTTC × S S GGGACCGTGG CCCTGGCACC ۵. æ د. TCGGTCTTCC AGCCAGAAGG ۵. Ce. > CAAGGGCCCA GTTCCCGGGT Ω. G × CGGCCTCCAC GCCGGAGGTG S æ TGCCAGAGGA ACCGICTCCI S S > H 2001 143

CAGGACTCTA GTCCTGAGAT >-ပ CTACAGTCCT GATGTCAGGA 0 CCCGGCTGTC GGGCCGACAG > æ ۵. ACGTGTGGAA TGCACACCTT ₽ × ACCAGCGGCG TGGTCGCCGC ပ S AGGCGCCCTG TCCGCGGGAC J ~ ပ CGTGGAACTC GCACCTTGAG ഗ z 3 GTGACGGTGT CACTGCCACA S > €-CCCCGAACCG GGGCTTGGC ш Q, AGGACTACTT TCCTGATGAA Ω 2101 177

GGTGGACAAG CCACCTGTTC × Ω > CCAACACCAA Corregerr ⊢ z CCTACATCTG CAACGTGAAT CACAAGCCCA GTGTTCGGGT Ω, × = GTTGCACTTA z > z GGATGTAGAC U >-GGCACCCAGA CCGTGGGTCT 0 ۲ TAGCAGCTTG ATCGTCGAAC J S ဟ CIGIGCCCIC GACACGGGAG ۵. AGCGTGGTGA TCGCACCACT > > CTCCCTCAGC SAGGGAGTCG ഗ . ഗ 2201 210

GGGGTTTTG CCCCCAAAC ۵. CITCCTCTTC GAAGGAGAAG £4. \_ CTGGCAGTCA GACCGTCAGT S ۵. GAGGACCCCC CTCCTGGGG ပ ے .. AGCACCTGAA TCGTCGACTT w م æ GTGGCACGGG CACCGIGCCC Ω, U ۵. ACTGITITGA GIGIGIACGG CACACATGCC ۵. O H TGACAAAACT ₽ × Ω GGTTTAGAAC CCANATCTTG O ഗ AAAGTTGAGC TTTCAACTCG w > × 2301 243

GGTACGTGGA CCATGCACCT TTCAAGTTGA AAGTTCAACT 3 z Œ. CCCTGAGGTC GGGACTCCAG w GCCACGAAGA CGGTGCTTCT w =GTGCACGTGA CACCTGCACT > 0 ATGCGTGGTG TACGCACCAC > > CTGAGGTCAC GACTCCAGTG > ധ GGAGTACTAG AGGGCCTGGG TCCCGGACCC œ CCTCATGATC Σ .. CCAAGGACAC GGTTCCTGTG Ω 2401 277

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GTGGCACCTG

TGTCGTTCGA

AAGAAGGAGA

GCTGCCGAGG

TGCGGAGGGC ACGACCTGAG

GATGTTCTGG

GCCTCTTGTT

TTACCCGTCG

CACCCTCTCG

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CETETECETS TETEGGGTA

CGCAGAAGAG

GAACGICTIC ICAIGCICCG IGAIGCAIGA GCCICTGCAC AACCACTACA

GCCACCAGGG

AAGAGCAGGT

2901

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CCAGGACTGG GGTCCTGACC CGAGAACCAC GCTCTTGGTG 0 CCCAGCGACA TCGCCGTGGA AGCGGCACCT CACCGTGGAC w 3 ۵. > ω ~ 0 GCGTCCTGCA AGGCAGCCC TCCCGTCGG GCCAGGACGT ACAGCAAGCT GGGTCGCTGT ۵. 0 ے 0 S CCGTGTGGTC AGCGTCCTCA CCCCATCGAG AAAACCATCT CCAAAGCCAA TCCGAAGATA TTTTGGTAGA GGTTTCGGTT GCCTGGTCAA AGGCTTCTAT TCGCAGGAGT TTCTTCCTCT >-\_ ~ Ce. > × ပ GGCACACCAG CGGACCAGTT CGACGGCTCC × > **-**> > H \_ œ GCCGCGGGAG GAGCAGTACA ACAGCACGTA CACGITCCAG AGGITGIIIC GGGAGGGICG GGGGIAGCIC TCGGACTGGA TGTCGTGCAT AGCCTGACCT TGCTGGACTC > ω ←  $\vdash$ Н \_ ഗ م ഗ CTCGTCATGT TCCCGGGAAG AGATGACCAA GAACCAGGTC CCCTCCCAGC CTTGGTCCAG ACCCCTCCCG ~ > >-۵. . 0 ب z GTGCAAGGTC TCCAACAAG CGCCCCTC AGGGCCTTC TCTACTGGTT CTACAAGACC  $\succeq$ W × œ z Σ م CGGCGTGGAG GTGCATAATG CCAAGACAAA CGGAGAACAA GGTTCTCTTT u > ப × œ ပ CACGTATTAC CTGAATGGCA AGGAGTACAA TCCTCATGTT AATGGGCAGC CCTGCCCCCA GGACGGGGT م z **>**-· == ۵. ω \_ GACTTACCGT SCCGCACCTC AGGTGTACAC TCCACATGTG  $\simeq$ GTGGGAGAGC ω ၒ > z ပ .. 2501 310 2601 343 2701 2801 377

AGAGGCCCAT TTATCATCGA TAAGCTTTAA ATTCGAMATT ပ ے۔ ഗ GGAGAGGGAC AATAGTAGCT ഗ GCGTCTTCTC GITTGACAGC CAAAAATAA CAATTGAGTA CAAACTGTCG **×** 0 TTGGTGATGT GTTAACTCAT >-= z CCGAGACGTG GITITITATI × ۔۔ • 200020000 GCTGCCGGGA TCTCAGGGAT TGCGAGCCAA CGGCGGCCCG AGTACGAGGC ACTACGTACT w I Σ CGACGGCCCT AGAGTCCCTA ACGCTCGGTT ഗ U ഗ CTTGCAGAAG C. > z CCGTCGTCCC  $\boldsymbol{\sigma}$ 0 AATAAGCATG TTCTCGTCCA TATTCGTAC  $\alpha$ S 0 3001 443 477 TGCGGTAGIT TATCACAGIT AAATTGCTAA CGCAGICAGG CACCGTGTAT GAAATCTAAC AATGCGCTCA TCGTCATCCT CGGCACCGTC ACCCTGGATG ACGCCATCAA ATAGTGTCAA TITAACGATI GCGTCAGTCC GTGGCACATA CTTTAGATIG TTACGCGAGT AGCAGTAGGA GGCGTGGCAG TGGGACCTAC Start Tet Resistance Coding Sequence 3101

CTGTAGGCAT AGGCTTGGTT ATGCCGGTAC TGCCGGGCCT CTTGCGGGAT ATCGTCCATT CCGACAGCAT CGCCAGTCAC TATGGCGTGC TGCTAGCGCT SACATCCGTA TCCGAACCAA TACGGCCATG ACGGCCCGGA GAACGCCCTA TAGCAGGTAA GGCTGTCGTA GCGGTCAGTG ATACCGCACG ACGATCGCGA 3201

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chain

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TCTCAGCTTA

TITITICITCI

TTCGAACGGG

CAACAATAAA

TITATGICIG TACTITITAG AGTAACGACT

AACCTATTCC

TCTCCATACT AGAGGTATGA

GAATTCAACT CTTAAGTTGA

101

201

301

401

TIGGATAAGG AAATACAGAC ATGAAAAATC TCATIGCIGA GITGITAITI AAGCITIGCCC AAAAAGAAGA AGAGICGAAI

CAGGTAGAGG CTCGTCAGTA GAGCAGTCAT CATGCGTTCA CGCTGATATC GCGACTATAG CAACTAACTA GTTGATTGAT AAAGAAGTTA TTGAAGCATC AACTTCGTAG TTTGTAACTA CAAACGCGTA AAACATTGAT GTTTGCGCAT z TITCITCAAT ACCAACAGCG TGGTTGTCGC TTTTAATGTA TATCAGCGAA ACAAAATAA AAAATTACAT TCTATTGCTA AGATAACGAT CGCGTTTTAC GCCCAAAATG GCGATTACGT CGCTAATGCA TGTTTTTTT GTTCGTTTTT CAAGCAAAAA Œ, > Ce. AGCGTTATAC GAGCTGCTGC TCGCAATATG CTCGACGACG ATAGTCGCTT TTGCATCTAT AACGTAGATA ഗ æ GACGTTACGA GCATTCCTGA CGACGATACG CGGCTCTGAA CTGCAATGCT CGTAAGGACT GCTGCTATGC GCCGAGACTT CGTAAAGAAG GCATTTCTTC Cz, Ø ATTATCGTCA TAATAGCAGT GCTGTCATAA AGTTGTCACG TCAACAGTGC CTTCTTATAG GAAGAATATC z AGCTTTGGAG TCGAAACCTC CCCGATGCCA CCGCGACAT GCTCCATTTC GGGCTACGGT GAATTATGAA CGACAGTATT CTTAATACTT CGAGGTAAAG CTTTTCAACA CGCAGGTAGA AGGGTATCTA GCGTCCATCT TCCCATAGAT GAAAAGTTGT GGCGCTGTA CTTGACACAC AAAAGTTAAT TTTTCAATTA TCACGTAAAA AGTGCATTTT

AATTTGACCA TTAAACTGGT Z TAGGAACTAT ATCGTTGATA CAGTCCTATA GTCAGGATAT Ω 0 TGCAGCGCAA ACGTCGCGTT S K S CACCATCACC GTGGTAGTGG € H ۲ GCGATAGGGT CGCTATCCCA > œ Ω GCCTCTGTGG CGGAGACACC ဗ > ഗ Ø GAGGGACAGG CTCCCTGTCC လ . ഗ AGTCCCCGAG TCAGGGGCTC ഗ ۵. S CAGITGACCC GTCAACTGGG ⋳ a O 501 56

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Signal

GTTCTGGGAC CAAGACCCTG လ TCTGGATCCG AGACCTAGGC S G TTCTCGCTTC AAGAGCGAAG [L œ ഗ CTGGAGTCCC GACCTCAGGG > Ö TCTCTCCACT AGAGAGGTGA  $\Xi$ J တ CTTCACCTCC GAAGTGGAGG S E Ĺ TACTGATTTA ATGACTAAAT > Н u GCTCCGAAAG CGAGGCTTTC × Q, Ø ACCAGGAAAA TGGTCCTTTT × ဇာ ATCAACAGAA TAGTTGTCTT O O 601 9

TGTCCCATGG ACAGGGTACC ပ O GGACGITTGG CCTGCAAACC ACCGTGCCGT TGGCACGGCA ۵, > ACAGTATAGC TGTCATATCG S >4 O ATTACTGTCA TAATGACAGT ပ > AAGCGTTGAA TTCGCAACTT H ⋖ GCCAGAAGAC CGGTCTTCTG Ω ω Δ, GCAGTCTGCA CGTCAGACGT O L S CTGACCATCA GACTGGTAGT H GGATTTCACT CCTAAAGTGA H CL, Ω 701 83

H CACACGGACG GTGTGCCTGC C TGCTTCTGTT ACGAAGACAA S 4 GAGCAGTIGA AATCIGGAAC TTAGACCTTG ပ တ CTCGTCAACT ... O Œ CGGTAGACTA GCCATCTGAT Ω တ Ω, TCATCTTCCC AGTAGAAGGG Œ, -CCATCTGTCT GGTAGACAGA > ഗ TGTGGCTGCA ACACCGACGT æ æ > TCAAACGAAC AGTTTGCTTG œ AAGGTGGAGA TICCACCICI > × 801 126

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901 TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA TCCTGTCGTT CAGTGTCTCG GGTCCTCTCA ω O GCCCATTGAG z G CGGGAGGTTA O CCACCTATTG Z Ω > CICCGGIIIC AIGICACCII 3 o 4 ш GATAGGGTCT œ ۵, ACTTATTGAA 160

GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC GCCTGCGAAG TCACCCATCA GGGCCTGAGC GITICAGAIG CGGACGCTIC AGIGGGIAGI CCCGGACICG > ω U **⊁** > × CCTGTCGTGG ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT = × ш Ω A × လ u ₽ GGACAGCACC TACAGCCTCA GCAGCACCCT **₊**1 € လ J S တ Ω 1001 193

1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTTAAT TAAATCCTCT ACGCCGGACG CATCGTGGCG AGCTCGGTAC CCGGGGATCT AGGCCTAACG CTCACAATTA ATTTAGGAGA TGCGGCCTGC GTAGCACCGC TCGAGCCATG GGCCCCTAGA TCCGGATTGC ပ မ GTTGTCCCCT ဇ œ z GTTTCTCGAA ČL, တ AGCGGGCAGT > 226

lambda to terminator^

CTCGGTTGCC GCCGGGCGTT TTTATTGTT GCCGACGCGC ATCTCGAATG AACTGTGGC GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGCAATGCTT BAGCCAACGG CGGCCCGCAA AAATAACAA CGGCTGCGCG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AAFAGCAGTG ACGTTACGAA 1201

CGCAATATGG CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGGG GGCGCTGTAC GAGGTAAAGC CCGATGCCAG CATTCCTGAC GACGATACGG GCGTTATACC GCGTTTTACT GGTTGTCGCC AACTAACTAG TCCATCTCCC CCGCGACATG CTCCATTTCG GGCTACGGTC GTAAGGACTG CTGCTATGCC 1301

1401 AGCTGCTGCG CGATTACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAAGTTAATC TTTTCAACAG CTGTCATAAA GTTGTCACGG CCGAGACTTA ICGACGACGC GCTAATGCAT TTCTTCAATA ACTTCGTAGG AGCAGTCATT TTTCAATTAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT

ATCAGCGAAA CAAAAATAAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCATTTTT CCCATAGATC TTAATACTTC TTGTTATAGC GTAAAGAAGA 1501 TAGTCGCTTT GTTTTTATTT TTTAATGTAT TTGTAACTAG TACGCAAGTT CACGTAAAA GGGTATCTAG AATTATGAAG AAGAATATCG CATTTCTTCT .a A I N X

STII Signal TIR-1

1601 TGCATCTATG TTCGTTTTT CTATTGCTAC AAACGCGTAC GCTGAGGTTC AGCTGGTGGA GTCTGGCGGT GGCCTGGTGC AGGCAGGGGG CTCACTCCGT GAGTGAGGCA ccedaccace rederecee G L < CAGACCGCCA ဗ တ CGACTCCAAG TCGACCACCT L V start heavy chain Б С TTTGCGCATG æ z ACGTAGATAC AAGCAAAAA GATAACGATG æ [z, æ

Inventor: REILLY ET AL. Docket No.: 11669.195USU1

Docket No.: 11669.1950SU1 Title: METHODS AND COMPOSITIONS FOR INCREASING ANTIBODY PRODUCTION

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TGGATTAACA ACCTAATTGT ATGGGTTGGA TACCCAACCT G > GGTCCGTCAG GCCCCGGGTA AGGGCCTGGA TCCCGGACCT J CGGGGCCCAT G ρ, CCAGGCAGTC 0 œ > CTATACCTTC ACCAACTATG GTATAAACTG CATATTTGAC z TGGTTGATAC >-Z GATATGGAAG E CAGCTTCTGG GTCGAAGACC တ TIGICCIGIG AACAGGACAC O S J 43

ACTIGICGGA TGAACAGCCT TACCTGCAGA ATGGACGTCT O u AAGCACAGCA TTCGTGTCGT Ø E ഗ TITICITIAG ACACCICCAA TGTGGAGGTT × ഗ ₽ AAAAGAAATC ... S AGCAAAGTGA TCGTTTCACT ₽ Cz, œ TAAAGTTTGC ATTTCAAACG × ţı. TATGCTGCGG ATACGACGCC A Z ACTTGGCTGG TGAACCGACC H Ω, [LI] CCTATACCGG GGATATGGCC 1801 7

GGGTCAAGGA CCCAGTTCCT ပ 0 ဗ TCGACGTCTG AGCTGCAGAC > Ω GTGACCATAA CACTGGTATT Ç, >-3 GCGGAAGAGC CGCCTTCTCG ഗ × œ TACACTIGCT ATGTGAACGA ω z > GGCGTGATAA CCGCACTATT > = ۵. TGCAAAGTAC ACGITTCATG > × æ AGATAATGAC TCTATTACTG O > > CTGTGACGGC GACACTGCCG æ €→ GCCCCCTGAG CGCGCGACTC ſΩ K æ 1901 110

CGGGACCCGA GCCCTGGGCT ပ GGCCACAGCG cécerercec K ₽ GCACCTCTGG CGTGGAGACC O ഗ E TCCTCCAAGA AGGAGGTTCT S × ഗ CCTGGCACCC GGACCGTGGG ρ, æ H CGGTCTTCCC GCCAGAAGGG Ω Ĺz, > TTCCCGGGTA AAGGCCCCAT Ω. G GGCCTCCACC CCGGAGGTGG ₽ တ Ø GGCAGAGGAG CCGTCTCCTC S S > ACCCTGGTCA TGGGACCAGT > H ₽ 2001 143

TACAGICCIC ATGTCAGGAG O CCGCCTGTCC GCCCGACAGG > 4 GCACACCTTC CGTGTGGAAG Œ, ₽  $\Xi$ CCAGCGGCGT GGTCGCCGCA > O S GGCGCCCTGA CCGCGGGACT .. Ø GTGGAACTCA CACCTTGAGT တ z 3 TGACGGTGTC ACTGCCACAG လ > CCCGAACCGG GGCTTGGCC Δ, ш GGACTACTTC CCTGATGAAG Œ, >-Ω GCCTGGTCAA CGGACCAGIT > u 2101 177

CAACACCAAG × z ACAAGCCCAG Terreggic ۵, AACGTGAATC TTGCACTTAG z > z CTACATCTGC GATGTAGACG C >-GCACCCAGAC CGTGGGTCTG ₽ O ₽ AGCAGCTTGG TCGTCGAACC ပ ᆸ S S TGTGCCCTCT ACACGGGAGA S ۵, > GCGTGGTGAC CGCACCACTG ₽ > > TCCCTCAGCA AGGGAGTCGT ഗ AGGACTCTAC **ICCTGAGATG** > H G 2201 210

TICCICITIC AAGGAGAAGG ACCGTCAGTC TGCCAGTCAG ഗ TCCTGGGGGG AGGACCCCC Ö හ u GCACCTGAAC CGTGGACTTG Œ ρ, Ä ACCGIGCCCA TGGCACGGGT Ω O ρ, GACAAACTC ACACATGCCC TGTGTACGGG ပ ₽ CTGTTTTGAG II. × Ω CAAATCTTGT GTTTAGAACA C တ × AAGTTGAGCC TTCAACTCGG W > GTGGACAAGA CACCTGTTCT × > 2301 243

AGTICAACTG TCAAGTTGAC CCTGAGGTCA GGACTCCAGT Œ CCACGAAGAC GGTGCTTCTG ш  $\Xi$ TGCGTGGTGG TGGACGTGAG ACCTGCACTC > Ω ACGCACCACC > > TGAGGTCACA ACTCCAGTGT > ω CCCGGACCCC GGCCTGGGG ۵, œ CTCATGATCT GAGTACTAGA Σ CAAGGACACC GTTCCTGTGG Ω CCCCAAAACC SGGGTTTTGG 2401 277

FIG. 4C

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CGTCCTGCAC GCAGGACGTG GTACGTGGAC GGCGTGGAGG TGCATAATGC CAAGACAAAG CCGCGGGAGG AGCAGTACAA CAGCACGTAC CGTGTGGTCA GCGTCCTCAC CCGCACCTCC ACGTATTACG GITCIGITTC GGCGCCCTCC ICGTCAIGIT GICGIGCAIG GCACACCAGI CGCAGAGIG L လ > > ₽ တ >o ப œ × H × z = ш > ဗ CATGCACCTG > 2501 310

CAAAGCCAAA GGGCAGCCCC CCCGTCGGGG Ω, o ပ GTTTCGGTTT × æ × CCTCCCAGCC CCCATCGAGA AAACCATCTC TTTGGTAGAG လ ۲ GGAGGGTCGG GGGTAGCTCT W ρ, æ ρ. L TGAATGGCAA GGAGTACAAG TGCAAGGTCT CCAACAAAGC GGTTGTTTCG Þ **×** z ACGITCCAGA > × U CCTCATGTTC × >-Сı ACTTACCGTT ဗ z 2601 CAGGACTGGC GTCCTGACCG O 343

GGTCGCTGTA CCAGCGACAT GGCTTCTATC CCGAAGATAG (z. ပ CTGCCCCCAT CCCGGGAAGA GATGACCAAG AACCAGGTCA GCCTGACCTG CCTGGTCAAA GGACCAGITI × ٦ ۲ CGGACTGGAC C ۲ L TTGGTCCAGT S > O z CTACTGGTTC × ₽ Σ GGGCCCTTCT (L) ы œ GACGGGGGTA S Ω, ۵. u CCACATGTGG GGTGTACACC H >-> GAGAACCACA CTCTTGGTGT O ۵, Œ 2701 377

CAGCAAGCTC GTCGTTCGAG ... × S TCTTCCTCTA CTGCCGAGGA AGAAGGAGAT .\_ cecereces serseacte sacsecter တ ပ CGACCTGAGG လ Ω L. GCGGAGGGCA > Δ, ۵, TACAAGACCA ATGTTCTGGT ۲ × CCTCTTGTTG GGAGAACAAC z z (L) TGGGAGAGCA ATGGGCAGCC TACCCGTCGG 0 G ACCCTCTCGT S ш 3 CGCCGTGGAG GCGCCACCTC (L) > Ø 2801 410

GAGAGGGACA S CTCTCCCTGT ഗ GCAGAAGAGC CGTCTTCTCG S × ō GCTCTGCACA ACCACTACAC TGGTGATGTG ₽ >-I CGAGACGTGT Z = J A GATGCATGAG CTACGTACTC ப I Σ TTGCAGAAGA GTACGAGGCA CATGCTCCGT > S ပ AACGTCTTCT S Ce. > **ĠCAGCAGGGG** CGTCGTCCCC G O O TCTCGTCCAC AGAGCAGGTG 3 α. ഗ ACCGTGGACA TGGCACCTGT Ω > ⊢ 2901 443

TATCATCGAT ATAGTAGCTA CTGCCGGGAT CTCAGGGATT GCGAGCCAAC GGCGGCCCGC AAAAAATAAC AATTGAGTAC AAACTGTCGA TTTGACAGCT CCCCCCCCCC TITITATIC ITAACTCAIG GAGTCCCTAA CGCTCGGTTG GACGGCCCTA TATTCGTACG ATAAGCATGC 0 CTCCGGGTAA GAGGCCCATT ပ Δ, 3001 477

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GOGGINGITI ATCACAGIIA AATTGCIAAC GCAGICAGGC ACCGIGIAIG AAAICIAACA AIGCGCICAI CGICAICCIC GGCACCGICA CCGTGGCAGT TGGCACATAC TITAGATIGI TACGCGAGIA GCAGIAGGAG CGTCAGTCCG TTAACGATTG TAGTGTCAAT CGCCATCAAA AAGCTTTAAT **LTCGAAATTA** 3101

GGGACCTACG ACATCCGTAT CCGAACCAAT ACGGCCATGA CGGCCCGGAG AACGC CCCTGGATGC TGTAGGCATA GGCTTGGTTA TGCCGGTACT GCCGGGCCTC 3201

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TAGCTACITIA AGTACGACAC CACAGIACCA GCCACIAGCG GICCCACGGC IGCGCGIAGA GCIGACGIGC CACGIGGIIA CGAAGACCGC AGICCGICGG 101 ATCGGAAGCT GTGGTATGGC TGTGCAGGTC GTAAATCACT GCATAATTCG TGTCGCTCAA GGCGCACTCC CGTTCTGGAT AATGTTTTT GCGCCGACAT

ATCGATGAAT TCATGCTGTG GTGTCATGGT CGGTGATCGC CAGGGTGCCG ACGCGCATCT CGACTGCACG GTGCACCAAT GCTTCTGGCG TCAGGCAGCC

TAGCCTTCGA CACCATACCG ACACGTCCAG CATTTAGTGA CGTATTAAGC ACAGCGAGTT CCGCGTGAGG GCAAGACCTA TTACAAAAA CGCGGCTGTA ATTCGAATCC CTGGCAAATA TTCTGAAATG AGCTGTTGAC AATTAATCAT CGAACTAGTT TAATGTGTGG AATTGTGAGC GGATAACAAT CCTATTGTTA GTATTGCCAA GACCGITTAT AAGACTITAC ICGACAACTG ITAAITAGTA GCTTGAICAA AITACACACC ITAACACTCG CATAACGGTT 201

GCTGCTGAAG CGACGACTTC ø TGCATGCACC AATCACTTTT TTAGTGAAAA ACGTACGTGG æ = CGCTGCTGGC GACCACAATG GCCGTTGCCC CGGCAACGGG Þ CTGGTGTTAC ₽ ₽ GCGACGACCG -1 GAAGATTTAT GAAATCACTG TTTAAAGTAA AAATTTCATT × CITCTAAATA CITTAGIGAC fkpA start ഗ 301 ATTCTAGAGG TAAGATCTCC

ACTGGGTGCC TCGCTGGGTC GTTACATGGA CAATGTACCT TGACCCACGG AGCGACCCAG Ö ø, ဇာ H CAAAAATGAC GATCAGAAAT CAGCTTATGC GTCGAATACG 4 >æ CTAGTCTTTA × O GITTITACIG Ω z × GCTGACAGCA AAGCAGCGTT TTCGTCGCAA Çz, Ø, Ø CGACTGTCGT ഗ Ω K TGCTACAGCT ACGATGTCGA æ E→ d CTGCAAAACC GACGITITGG × Þ 401 29

CAMACTCTCC GTTTGAGAGG GATGCATTTG CTGATAAGAG GACTATTCTC Ω CTACGTAAAC ſz, 4 TGGTGTTCAG ACCACAAGTC O > Ö GATAAAGATC AGCTGATCGC TCGACTAGCG H ... CTATTTCTAG O Ω × CATCAAACTG GTAGTTTGAC H × 1-4 AAAGAACAAG AAAAACTGGG TTTTTGACCC J × TTTCTTGTTC O (ca) AAACTCTCTA TTTGAGAGAT ഗ z 501 62

TTCTGCTCAG GCGAAGATGG AAAAAGACGC GGCTGATAAC GAAGCAAAAG CTTCGTTTTC CCGACTATTG Ω Ø CGCTTCTACC TTTTTCTGCG Ω Σ × AAGACGAGTC O Ø ഗ Tresagere ecercaagre CGCACTTCAG × AAGCTTCGAG Ø 回 TCTACAAGCA AGATGTTCGT 4 O H GACCAAGAGA TCGAACAGAC AGCTTGTCTG 0 Œ CIGGITCICI ω 601 95

GCCGGTAAAG GCGAAGCACC CGCTTCGTGG K CGGCCATTTC ဗ GGTAGTAGAA CCATCATCTT TCAACTGGTC TGGTTTATCA CITITIGGAGA AGTIGACCAG ACCAAATAGI >4 > ы Ö GAAAACCTCT လ H × TITGCCAAAG AGAAAGGTGT TCTTTCCACA Ö × AAACGGTTTC × 4 GGCGCTCTTT CCGCGAGAAA 回 œ GTAAAGAGTA CATTTCTCAT G 701 129

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CAGC G	ATA( TAT(	TGTTG	GAAAGACAGC GATACTGTTG TAGTGAACTA CTTTCTGTCG CTATGACAAC ATCACTTGAT		CTGATCGACG GACTAGCTGC	GTAAAGAGTT CATTTCTCAA	CGACAACTCT GCTGTTGAGA	TACACCCGTG	grgaaccgcr cactrggcga	TTCTTTCCGT AAGAAAGGCA
162 K D S D T V V N Y	ΛΛΛ	>	N N	K D	L I D G	KGT LIDG KEF DNS YTRG EPL SFR	N N	۲. ۲.	-B	ς Επ σς
901 CTGGACGGTG TTATCCCGGG TTGGACAGAA	ccess mes	TTGG	ACAGAA	GGTCTGAAGA ACATCAAGAA AGGCGGTAAG ATCAAACTGG TTATTCCACC AGAACTGGCT TACGGCAAAG	ACATCAAGAA	AGGCGGTAAG	ATCAAACTGG	TTATTCCACC	AGAACTGGCT	TACGGCAAAG
GACCTGCCAC AATAGGGCCC AACCTGTCTT CCAGACTTCT TGTAGTTCTT TCGGCCATTC TAGTTTGACC AATAAGGTGG TCTTGACCGA ATGCCGTTTC	BGGCC AACCT	MCCI	GICIT	CCAGACTTCT	TGTAGTTCTT	TCCGCCATTC	TAGITIGACC	AATAAGGTGG	TCTTGACCGA	ATGCCGTTTC
195 L D G V I P G W T E	ტ ლ	<b>≥</b>		G L K N I K K G G K I K L V I P P E L A Y G K A	H X	⊭ უ	r r r	а а	ल च	ж У
1001 CGGGTGTTCC GGGGATCCCA CCGAATTCTA	NICCCA CCGAAI	CCGAAT	TCTA	CCCIGGIGIT IGACGIAGAG CIGCIGGAIG IGAAACCAGC GCCGAAGGCI GAIGCAAAGC CGGAAGCIGA	TGACGTAGAG	CTGCTGGATG	TGAAACCAGC	GCCGAAGGCT	GATGCAAAGC	CGGAAGCTGA
GCCCACAAGG CCCCTAGGGT GGCTTAAGAT GGGACCACAA ACTGCATCTC GACGACCTAC ACTITGGTCG CGGCTTCCGA CTÁCGTTTCG GCCTTCGACT	ragger gectta	GGCTTA	AGAT	GGGACCACAA .	ACTGCATCTC	GACGACCTAC	ACTITIGGTCG	CGCCTTCCGA	CTACGTTTCG	GCCTTCGACT
229 GVP GIP PNST	2 Q Q	ار اند اند	<b>€</b> →	LVF DVE LLDV KPA PKA DAKP EAD	ы >	л о т т	X P A	A A	о х ч	E A D
1101 TGCGAAAGCC GCAGATTCTG CTAAAAATA	vircis craaaaa	CTABABA		AAAGCTAGC						
ACGCTITICGG CGTCTAAGAC GAITITITAI	TABBAC GATTITI	GATTTTT		TTTCGATCG						

FIG. 5B

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AAAAAGAAGA AGAGTCGAAT TTTTTTTTT AAGCTTGCCC CAACAATAAA TTCGAACGGG GITGITATIT TCATTGCTGA AGAGGTATGA AACCTATTCC TITTATGTCTG TACTTTTTAG AGTAACGACT ITGGATAAGG AAATACAGAC ATGAAAATC TCTCCATACT GAATTCAACT CTTAAGTTGA ECORI CCCAGGTAGA AGCTITIGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG CTIGACACAC GCGICCAICI ICGAAACCIC IAAIAGCAGI GACGIIACGA AGCGIIAIAC CGCGIIIIIAC IGGIIGICGC CAACIAACIA GICCAICICC GAACTGTGTG 101

GGCCGCTGTA CGAGGTAAAG CCCGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCAGTA GCTCCATTIC GGGCTACGGT CGTAAGGACT GCTGCTAIGC CTCGACGACG CGCTAAIGCA ITTCTTCAAT AACITCGTAG GAGCAGTCAI CCCCCGACAT 201

CATGCGTTCA TITGIAACTA GIACGCAAGI AAACATTGAT TGTTTTTATT TTTTATGTA TCAACAGIGC CGGCTCTGAA IATCAGCGAA ACAAAAATAA AAAATTACAT GCTGTCATAA AGTTGTCACG GCCGAGACTT ATAGTCGCTT CGACAGTATT CTTTTCAACA GAAAAGTTGT AAAAGTTAAT TTTTCAATTA 301

CAAGCAAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG GITCGITIII ICIAIIGCIA CAAACGCGIA CGCIGAIAIC anti-TF|light chain^ æ > Œ. TTGCATCTAT TITCTIAIAG CGIAAAGAAG AACGIAGAIA တ K AGGGTATCTA GAATTATGAA AAAGAATATC GCATTTCTTC STII signal TIR 7 Œ X start TCCCATAGAT CTTAATACTT TCACGTAAAA AGTGCATTTT 401

GITÉTCGATA GACTIGACCA GTCGCGACAT CAAGAGCTAT CTGAACTGGT 3 z S CAGCGCTGTA Ω œ CACCATCACC TGCAGAGCCA ACGTCTCGGT œ GTGGTAGTGG H Н E CTCCCTGTCC GCCTCTGTGG GCGATAGGGT CGCTATCCCA œ Ω CGGAGACACC > ഗ GAGGGACAGG တ J ഗ AGTCCCCGAG TCAGGGGCTC တ Ω, 501 CAGATGACCC GTCTACTGGG Σ O 26

TCTGGATCCG GTTCTGGGAC AAGAGCGAAG AGAĆCTAGGC CAAGACCCTG ပ ഗ TTCTCGCTTC Œ, œ ഗ CTATGCTACT AGTCTCGCTG AAGGAGTCCC TCAGAGCGAC TTCCTCAGGG > ပ Œ æ ... S GATACGATGA æ ACCAGGAAAA GCTCCGAAAG TACTGATTTA CGAGGCTTTC ATGACTAAAT Н ᆸ × ۵. æ TGGTCCTTTT × ပ ۵, 601 ATCAACAGAA TAGTTGTCTT O O 9

ACAGGGTACC TGTCCCATGG ပ o GAGTCTCCAT GGACATTTGG CCTGTAAACC E CTCAGAGGTA 3 တ Œ TTCGCAACTT ATTACTGTCT TCAGCACGGA AGTCGTGCCT ပ I o TAATGACAGA U >-AAGCGTTGAA ۲ Ø CTGACCATCA GCAGTCTGCA GCCAGAAGAC CGGTCTTCTG Ω ω Q, CGTCAGACGT O ᆸ ഗ GACTGGTAGT S E GGATTACACT CCTAATGTGA E Ω 701 93

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GIGIGGCIGC CACACGGACG O TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT TTAGACCTTG ACGAAGACAA တ ပ ഗ CTCGTCAACT ... O (LI) CGGTAGACTA Ω ഗ Q, ACACCGACGT GGTAGACAGA AGTAGAAGGG O. Ŀ Н > ഗ Д Ø 4 801 AAGGTGGAGA TCAAACGAAC AGTTTGCTTG E ø; × TTCCACCTCT வ > ×

AGGACAGCAA TCCTGTCGTT × ഗ Ω GTCACAGAGC CAGTGTCTCG O ш ۲ ک CCAGGAGAGT GETCCTCTCA တ ш 0 CGGGTAACTC GCCCATTGAG ഗ z Ö GCCCTCCAAT CGGGAGGTTA ø A L GGTGGATAAC CCACCTATTG z Ω > ATGTCACCTT GAGGCCAAAG TACAGTGGAA × 3 o CTCCGGTTTC × A B CTATCCCAGA GATAGGGTCT œ Δ, >4 TGAATAACTT ACTTATTGAA z z 901 160

GGGCCTGAGC CCCGGACTCG တ G TCACCCATCA AGTGGGTAGT = AAAGCAGACT ACGAGAAACA CAAAGTCTAC GCCTGCGAAG CGGACGCTTC (±1 U GTTTCAGATG > × TGCTCTTTGT Ξ × w TTTCGTCTGA Ω GACGCTGAGC CTGCGACTCG လ ᆸ E GCAGCACCCT CGTCGTGGGA E ഗ TACAGCCTCA ATGTCGGAGT ᆸ ഗ GGACAGCACC CCTGTCGTGG ₽ S Ω 1001 193

CAACAGGGGA GAGTGTTAAT TAAATCCTCT ACGCCGGACG CATCGTGGCG AGCTCGGTAC CCGGGGATCT AGGCCTAACG TCCGGATTGC CTCACAATTA ATTTAGGAGA TGCGGCCTGC GTAGCACCGC TCGAGCCATG GGCCCTAGA 0 ပ ω GTTGTCCCCT œ z CAAGAGCTT GTTTCTCGAA ſĿ, ഗ × TCGCCCGTCA AGCGGGCAGT > 1101 226

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ITITIATIGIT GCCGACGCGC ATCTCGACTG CACGGTGCAC CAATGCTTCT GGCGTCAGGC AGCCATCGGA AGCTGTGGTA AAAATAACAA CGGCTGCGCG TAGAGCTGAC GTGCCACGTG GTTACGAAGA CCGCAGTCCG TCGGTAGCCT TCGACACCAT CICGGIIGCC GCCGGGCGII SAGCCAACGG CGGCCCGCAA 1201

TGGCTGTGCA GGTCGTAAAT CACTGCATAA TTCGTGTCGC TCAAGGCGCA CTCCCGTTCT GGATAATGTT TTTTGCGCCG ACATCATAAC GGTTCTGGCA CCAAGACCGT TGTAGTATTG CCAGCATTIA GIGACGIAIT AAGCACAGCG AGIICCGCGI GAGGGCAAGA CCIAITACAA AAAACGCGGC ACCGACACGT 1301

TAGGATCTAG AATTATGAAG TTAATACTTC CTCGCCTAIT GITAAITCGA AICCTAGAIC GTGGAATTGT GAGCGGATAA CAATTAAGCT TTACTCGACA ACTGTTAATT AGTAGCTTGA TCAAATTACA CACCTTAACA TGACAATTAA TCATCGAACT AGTTTAATGT AATGAGCTGT 1401 AATATTCTGA TTATAAGACT

Start STII signal TIR

O TITGICITII CIATAGCIAC AAACGCGIAC GCIGAGGIIC AGCIGGIGGA GICTGGCGGI GGCCIGGIGC CCGGACCACG ... TITGCGCATG CGACTCCAAG TCGACCACCT CAGACCGCCA G ^anti-TF heavy chain [12] > ᆸ O > ш æ > ⋖ z GATATCGATG ø н ACGGAGATAC AAACAGAAAA ഗ Cz, > TGCCTCTATG ഗ 4 CGTTCCTACT GCAAGGATGA ... J G, 1501 AAGAATATTG TTCTTATAAC z ×

Inventor: REILLY ET AL.
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CTCACTCCGT TIGTCCTGTG CAGCTTCTGG CTTCAATATT AAGAGTACT ACATGCACTG GGTCCGTCAG GCCCCGGGTA AGGGCCTGGA TCCCGGACCT AAACACAGCA TITGIGICGI ... ပ CGGGGCCCAT TGTTAAGGTT G O 24

CCGTGCCACT ATAAGCGCTG ACAATTCCAA CCAGGCAGTC TATTCGCGAC > TGTACGTGAC GCACGGTGA  $\Xi$ TTCCTCATGA ATACTGGGCT TCAAGGTCCT CAACACGATC TATGACCCGA AGTTCCAGGA M GAAGTTATAA z [z, GTTGTGCTAG GTCGAAGACC တ AACAGGACAC TTGATTGATC CAGAGCAAGG GTCTCGTTCC ပ AACTAACTAG GAGTGAGGCA æ .\_ ഗ 1701 ATGGGTTGGA TCGGTCCCCC TACCCAACCT G

1601 AGCCAGGGG

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S Ø ഗ ~ œ Ω O ſz, × ρ, **--**H z ပ O ω Ω > 3 2

GGAACCCTGG CCTTGGGACC L CTGGGGTCAA GACCCCAGTT O ပ GCGTGCTGAG GACACTGCCG TCTATTATTG TGCTCGAGAC ACGCCCGCTT ACTTCGACTA TGAAGCTGAT >-Ω [II. TGCCGGCGAA Ø æ AGATAATAAC ACGAGCTCTG Ω Ω: æ O >->-CTGTGACGGC æ ₽ CGCACGACTC ξı] 4 1801 TACCTGCAGA TGAACAGCCT ACTIGICGGA ഗ z ATGGACGTCT >-103

CGACGGACCA GCTGCCTGGT O GCGCCCTGG CGCCGGGACC ပ A TGGGGGCACA ACCCCCGTGT E ပ ပ CCCTCCTCCA AGAGCACCTC TCTCGTGGAG S ۲ S GGGAGGAGGT × S တ CCCCCTGGCA GGGGGACCGT Ø ᆸ Ω, CATCGGTCTT GTAGCCAGAA CZ. > S TGGTTCCCGG ACCAAGGGCC ဗ × CTCGGCCTCC GAGCCGGAGG တ ø S AGTGGCAGAG TCACCGTCTC ഗ > 1901 137

GAGTCCTGAG CTCAGGACTC G တ TCCTACAGTC AGGATGTCAG AAGGGCCGAC TTCCCGGCTG 4 Δ, CGTGCACACC GCACGTGTGG E⊸ = > TGACCAGCGG AGTCCGCGGG ACTGGTCGCC တ H TCAGGCGCCC æ Ö GTCGTGGAAC CAGCACCTTG z 3 ഗ CGGTGACGGT GCCACTGCCA E > AAGGGGCTTG TTCCCCGAAC ω p, CAAGGACTAC GTTCCTGATG Ω ×

CAGCAACACC AAGGTGGACA TICCACCIGI Greenge GACCTACATC TGCAACGTGA ATCACAAGCC CTGGATGTAG ACGTTGCACT TAGTGTTCGG × = z > z ပ GACTGTGCCC TCTAGCAGCT TGGGCACCCA ACCCGTGGGT O ₽ Ö CTGACACGGG AGATCGTCGA ഗ တ ഗ > 2101 TACTCCCTCA GCAGCGTGGT CGTCGCACCA > > ഗ ATGAGGGAGT ᆸ 203

GICTICCICI ICCCCCCAAA AGGGGGGTTT CAGAAGGAGA CCCTGGCAGT GGGACCGTCA ഗ p, ပ CCAGCACCTG AACTCCTGGG GGTCGTGGAC TTGAGGACCC ... J (LI) Ω, Æ d TGTGACAAA CTCACACATG CCCACCGTGC GGGTGGCACG O Ω, ۵, GAGTGTGTAC ۲ ı ACACTGTTTT × Δ ပ GCCCAAATCT CGGGTTTAGA S × AGAAAGTTGA TCTTTCAACT × 2201 237

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GACCATGCAC CTGGTACGTG TCAAGTTCAA AGTTCAAGTT CTGGGACTCC GAGCCACGAA GACCCTGAGG ω ρ, CTCGGTGCTT ω = TGGTGGACGT ACCACCTGCA Ω CCCTGAGGTC ACATGCGTGG GGGACTCCAG TGTACGCACC ပ മ ACCCAAGGAC ACCCTCATGA TCTCCCGGAC AGAGGGCCTG ഗ TGGGAGTACT Σ ۲ IGGGTTCCTG 2301 270

GTGGTCCTGA CACCAGGACT Δ 0 GTGGCAGGAC CACCGTCCTG > E TCAGCGTCCT AGTCGCAGGA H > S TACCGTGTGG GTTGTCGTGC ATGGCACACC > œ CAACAGCACG E တ z TCCTCGTCAT AGGAGCAGTA O ш AAGCCGCGGG Tregecece œ Δ, TGCCAAGACA ACGGTTCTGT ۲ × æ GACGCCTCC AGGTGCATAA TCCACGTATT = CTGCCGCACC ω Ö 2401 303

CCCGAGAACC GGCTCTTGG ω œ ANAGGGCAGC Trircccerce O G CTCCAAAGCC GAGGTTTCGG K × ഗ GCCCCCATCG AGAAACCAT TCTTTTGGTA E × CGGGGGTAGC Œ Н Ω, AGCCCTCCCA TCGGGAGGGT Ω, ... K TCTCCAACAA TTCACGTTCC AGAGGTTGTT × z တ AAGTGCAAGG × ပ CAAGGAGTAC GTTCCTCATG > ш × CCGACTTACC GGCTGAATGG z 2501 337

CATCGCCGTG GTAGCGGCAC CTGCCTGGTC AAAGGCTTCT ATCCCAGCGA TAGGGTCGCT GACGGACCAG TITCCGAAGA Œ4 ೮ > Ö AGAGATGACC AAGAACCAGG TCAGCCTGAC AGTCGGACTG E H တ TTCTTGGTCC O z TCTCTACTGG ₽ Σ: ω CATCCCGGGA GTAGGGCCCT (L) o: ഗ ACCCTGCCCC TGGGACGGG ρ, H ACAGGTGTAC TGTCCACATG > 0 2601 370

CTCACCGTGG GAGTGGCACC CTACAGCAAG GATGTCGTTC တ GGAAGAAGGA TCCGACGCT CCTTCTTCCT [z, Œ AGGCTGCCGA G Ω CGTGCTGGAC GCACGACCTG Ω u > CCACGCCTCC GGTGCGGAGG ۵ ₽ AACTACAAGA TTGATGTTCT × GCCGGAGAAC CGCCTCTTG z ப ρ, GCAATGGGCA CGTTACCCGT ပ z GAGTGGGAGA CTCACCCTCT w 3 ω 2701 403

GIGGCAGCAG GGGAACGICI ICTCAIGCIC CGIGAIGCAT GAGGCICIGC ACAACCACIA CACGCAGAAG AGGCICICCC IGICICCGGG ACAGAGGCCC TCGGAGAGGG GIGCGICTIC × O ₽ TGTTGGTGAT × z CTCCGAGACG L 4 ш GCACTACGTA = Σ > AGAGTACGAG O CCCTTGCAGA z CACCGTCGTC O O 3 2801 ACAAGAGCAG TGTTCTCGTC တ 437

CTATTCGAAA TAAATAAGCA TGCGACGGCC CTAGAGTCCC TAACGCTCGG TTGCCGCCGG GCGTTTTTTA TTGTTAACTC ATGTTTGACA GCTTATCATC GATAAGCTTT CGAATAGTAG ATTTATTCGT ACGCTGCCGG GATCTCAGGG ATTGCGAGCC AACGGCGGCC CGCAAAAAT AACAATTGAG TACAAACTGT 2901

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TCTCAGCTTA GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAATC TCATTGCTGA GTTGTTATTT AAGCTTGCCC AAGAAGAAGA TTTTTCTTCT CAACAATAAA TTCGAACGGG CITAAGITIGA AGAGGIATGA AACCIAITICC IITAIGICIG TACITITITAG AGIAACGACI

CAGGTAGAGG CAACTAACTA GICCAICICC GTTGATTGAT GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG CITGACACAC GCGICCAICI ICGAAACCIC IAAIAGCAGI GACGITACGA AGCGITAIAC CGCGITITIAC IGGITGICGC 101

CTCGTCAGTA AACITICGTAG GAGCAGTCAT TTGAAGCATC CCCGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAGAAGTTA GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT CGAGGTAAAG GCTCCATTTC GGCGCTGTA CCCGCGACAT 201

GTACGCAAGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA TTTGTAACTA TITITAATGIA GCTGTCATAA AGTTGTCACG GCCGAGACTT ATAGTCGCTT TGTTTTTATT AAAAGTTAAT CTTTTCAACA TITTCAATTA GAAAAGTTGT 301

CAAGCAAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG TCACGIAAAA AGGGIAICIA GAATIAIGAA AAAGAAIAIC GCATIICIIC IIGCAICIAI GIICGIIIII ICIAIIGCIA CAAACGCGIA CGCIGAIAIC Ω anti-tissue factor light chain^ E ſz, > ſz, TITCITIATAG CGTAAAGAAG AACGTAGATA Σ တ 4 . .3 .-Start STII signal TIR 7 × TCCCATAGAT CTTAATACTT AGTGCATTTT 401

GACTTGACCA TGCAGAGCCA GTCGCGACAT CAAGAGCTAT CTGAACTGGT 3 z GTTCTCGATA ഗ × CAGCGCTGTA Ω œ ACGTCTCGGT Ø œ CTCCCTGTCC GCCTCTGTGG GCGATAGGGT CACCATCACC GTGGTAGTGG ₽ CGCTATCCCA œ Ω CGGAGACACC G > ഗ GAGGGACAGG ഗ ᆈ ഗ AGTCCCCGAG TCAGGGGCTC ഗ ρ, တ CAGATGACCC GTCTACTGGG Σ o 501 56

GITCIGGGAC CAAGACCCTG ဗ TACTGATITA CTATGCTACT AGTCTCGCTG AAGGAGTCCC TTCTCGCTTC TCTGGATCCG TTCCTCAGGG AAGAGCGAAG AGACCTAGGC တ ſz, ∞; တ Ω, > ပ CGAGGCTTTC ATGACTAAAT GATACGATGA TCAGAGCGAC æ S E Ø >-**≻** H GCTCCGAAAG × Δ, æ ACCAGGAAAA TGGTCCTTTT × G Д ATCAACAGAA TAGTTGTCTT O O 601 9

ACAGGGTACC TGTCCCATGG ပ O GGACATTTGG CCTGTAAACC Ö (z, GAGTCTCCAT CTCAGAGGTA 3 Δ, S GGATTACACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTCT TCAGCACGGA AGTCGTGCCT ပ × o AAGCGTTGAA TAATGACAGA U >-> ₽ A H CGGTCTTCTG Ω ω ۵, CGTCAGACGT ... တ GACTGGTAGT E CCTAATGTGA 701 8

CACACGGACG GTGTGCCTGC ပ TGCTTCTGTT ACGAAGACAA ഗ AATCTGGAAC TTAGACCTTG Ö ഗ GAGCAGTTGA CGGTAGACTA CTCGTCAACT ... o GCCATCTGAT Ω ഗ ρ, TCATCTTCCC GGTAGACAGA AGTAGAAGGG <u>г</u> CCATCTGTCT > တ TCAAACGAAC TGTGGCTGCA AGTITGCITG ACACCGACGI 4 > 04 TTCCACCTCT 801 AAGGTGGAGA × 126

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GTCACAGAGC AGGACAGCAA GGCCTGAGC CCCGGACTCG တ ഗ ب Ω CAGTGTCTCG AGTGGGTAGT TCACCCATCA × CCAGGAGAGT GGTCCTCTCA CGGACGCTTC GCCTGCGAAG (L) ы ပ œ CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC GCCCTCCAAT CGGGTAACTC GCCCATTGAG CAAAGTCTAC GTTTCAGATG > ပ × CGGGAGGTTA ACGAGAAACA TGCTCTTTGT = O × H ш CCACCTATTG AAAGCAGACT TTTCGTCTGA Ω Ω æ > GACGCTGAGC ATGTCACCTT CTGCGACTCG တ 3 ., o ₽ CTCCGGTTTC GCAGCACCCT CGTCGTGGGA × Eæ လ GATAGGGTCT TACAGCCTCA ATGTCGGAGT œ .\_ ۵, လ TGAATAACTT GGACAGCACC CCTGTCGTGG ACTTATTGAA ſı, z ഗ z Ω 901 1001 160 193

AGGCCTAACG TCCGGATTGC AGCTCGGTAC CCGGGGATCT CTCACAATTA ATTTAGGAGA TGCGGCCTGC GTAGCACCGC TCGAGCCATG GGCCCCTAGA CATCGTGGCG ACGCCGGACG TAAATCCTCT GAGTGTTAAT 0 U CAACAGGGGA GITGICCCCT Ö ∞: z GTTTCTCGAA CAAGAGCTT (z, ഗ AGCGGGCAGT TCGCCCGTCA > လ 1101 226

lambda to terminator^

AGCTGTGGTA GOCGTCAGGC AGCCATCGGA TCGGTAGCCT CCGCAGTCCG CGGCCCGCAA AAAATAACAA CGGCTGCGCG TAGAGCTGAC GTGCCACGTG GTTACGAAGA TITIAITIGIT GCGACGCGC ATCTCGACTG CACGGTGCAC CAATGCTTCT CTCGGTTGCC GCCGGGCGTT SAGCCAACGG 1201

ACATCATAAC GGTTCTGGCA TGTAGTATTG CCAAGACCGT CACTGCATAA TICGIGICGC ICAAGGCGCA CICCCGITCI GGATAAIGIT ITTTGCGCCG CCAGCATTTA GTGACGTATT AAGCACAGCG AGTTCCGCGT GAGGGCAAGA CCTATTACAA AAAACGCGGC GGTCGTAAAT TGGCTGTGCA ACCGACACGT 1301

TTATAAGACT TTACTCGACA ACTGTTAATT AGTAGCTTGA TCAAATTACA CACCTTAACA CTCGCCTATT GTTAATTCGA ATCCTAGATC TTAATACTTC 1401 AATATTCTGA AATGAGCTGT TGACAATTAA TCATCGAACT AGTTTAATGT GTGGAATTGT GAGCGGATAA CAATTAAGCT TAGGATCTAG AATTATGAAG

Start STII signal TIR 3

O CCGGACCACG 1501 AAGAATATTG CGTTCCTACT TGCCTCTATG TTTGTCTTTT CTATAGCTAC AAACGCGTAC GCTGAGGTTC AGCTGGTGGA GTCTGGCGGT GGCCTGGTGC > ... CAGACCGCCA Ö S GCAAGGATGA ACGGAGATAC AAACAGAAAA GATATCGATG TTTGCGCATG CGACTCCAAG TCGACCACCT 臼 > L > heavy chain with cys to ser in hinge anti-tissue factor Σ ഗ 4 . Ц TTCTTATAAC z

GGTCCGTCAG GCCCCGGGTA AGGGCCTGGA TCCCGGACCT .\_ CGGGGCCCAT ပ CCAGGCAGTC O œ > TTGTCCTGTG CAGCTTCTGG CTTCAATATT AAGGAGTACT ACATGCACTG TGTACGTGAC I Σ TTCCTCATGA ω GAAGTTATAA z ſz, GTCGAAGACC O S 4 AACAGGACAC ပ တ GAGTGAGGCA CTCACTCCGT æ u ഗ 1601 AGCCAGGGG regereeec G O Ω, 37

# FIG. 7B

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TTTGTGTCGI E CCGTGCCACT ATAAGCGCTG ACAATTCCAA GGCACGGTGA TATTCGCGAC TGTTAAGGTT 4 တ æ 1701 ATGGGTTGGA TTGATTGATC CAGAGCAAGG CAACACGATC TATGACCCGA AGTTCCAGGA TCAAGGTCCT O Cz, ATACTGGGCT ۵, > GTTGTGCTAG . Ez GTCTCGTTCC ဗ O ш AACTAACTAG Ω TACCCAACCT Ö 3

GGAACCCTGG CCTTGGGACC u E CTGGGGTCAA GACCCCAGTT O Ö TGAACAGCCT GCGTGCTGAG GACACTGCCG TCTATTATTG TGCTCGAGAC ACGGCCGCTT ACTTCGACTA TGAAGCTGAT Ω TGCCGGCGAA A A L CTGTGACGGC AGATAATAAC ACGAGCTCTG Ω œ Þ >-> > æ €→ Ω CGCACGACTC 臼 æ œ ACTIGICGGA တ z 1801 TACCTGCAGA ATGGACGTCT O **>**-103

CGACGGACCA GCIGCCIGGI ... ပ GCGGCCCTGG CGCCGGGACC ဗ 4 TGGGGGCACA GGGAGGAGGT TCTCGTGGAG ACCCCCGTGT ₽ ပ ဗ AGAGCACCTC ഗ E လ CATCGGTCTT CCCCCTGGCA CCCTCCTCCA × ഗ တ م GGGGGACCGT ø .\_ ρ, GTAGCCAGAA > တ 1901 TCACCGTCTC CTCGGCCTCC ACCAAGGGCC TGGTTCCCGG ပ × GAGCCGGAGG တ æ ഗ AGTGGCAGAG 137

CTCAGGACTC GAGTCCTGAG u G ഗ TICCCGGCTG TCCTACAGTC AGGATGTCAG O AAGGGCCGAC ۵, CGTGCACACC GCACGTGTGG => TCAGGCGCCC TGACCAGCGG CAGCACCTIG AGICCGCGGG ACIGGICGCC O တ ₽ 4 O GTCGTGGAAC z 3 S CGGTGACGGT GCCACTGCCA E > TTCCCCGAAC AAGGGGCTTG Ω, (L) Ω, GTTCCTGATG CAAGGACTAC Ω × 2001 170

CAGCAACACC AAGGTGGACA TTCCACCTGT GTCGTTGTGG z TGCAACGTGA ATCACAAGCC TAGTGTTCGG ρ, × I ACGTTGCACT Z > z ပ CTGGATGTAG GACCTACATC -× £ TGGGCACCCA ACCCGTGGGT O H ပ TCTAGCAGCT CTGACACGGG AGATCGTCGA တ S GACTGTGCCC ۵, > ₽ GCAGCGTGGT CGTCGCACCA > ഗ ATGAGGGAGT TACTCCCTCA . ഗ >-2101 203

TCCCCCCAAA CAGAAGGAGA AGGGGGGTTT GICTICCICT (z, GGGACCGTCA CCCTGGCAGT ۵, ප TOTOACAAAA CTCACACTAG TCCACCGTCT CCAGCACCTG AACTCCTGGG GAGTGTGATC AGGTGGCAGA GGTCGTGGAC TTGAGGACCC ... .-'Hinge cys to ser ဟ Δ, ACACTGTTTT G U GCCCAAATCT CGGGTTTAGA × 2201 AGAAAGTTGA TCTTTCAACT 237

ser \*Hinge cys to

CTGGTACGTG GACCATGCAC 3 GACCCTGAGG TCAAGTTCAA CIGGGACTCC AGTICAAGIT (z, CCCTGAGGTC ACATGCGTGG TGGTGGACGT GAGCCACGAA CTCGGTGCTT I တ GGGACTCCAG TGTACGCACC ACCACCTGCA Ω > ۸ ۸ ပ ы Δ, TCTCCCGGAC AGAGGGCCTG TGGGAGTACT ACCCAAGGAC ACCCTCATGA TGGGTTCCTG × 270

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CACCGTCCTG CACCAGGACT GTGGTCCTGA Ω GTGGCAGGAC H ₽ CAACAGCACG TACCGTGTGG TCAGCGTCCT GITGICGIGC AIGGCACACC AGICGCAGGA H > တ > œ တ Z TGCCAAGACA AAGCCGCGGG AGGAGCAGTA TTCGGCGCCC TCCTCGTCAT O ш œ ρ, ACGGTTCTGT K 2401 GACGCCTCC AGGTCCATAA TCCACGTATT × CTGCCGCACC ပ Ω 303

CCCGAGAACC GGCTCTTGG (LI) œ AAAGGGCAGC TTICCCGTCG o CTCCAAAGCC GAGGTTTCGG 4 × တ AGAAAACCAT TCTTTTGGTA E GCCCCCATCG CGGGGGTAGC Н ρ, 4 AGCCCTCCCA TCGGGAGGGT Д H 4 TCTCCAACAA AGAGGTTGTT × z တ TTCACGTTCC AAGTGCAAGG × ပ CAAGGAGTAC GTTCCTCATG >ω GGCTGAATGG CCGACTTACC ပ z 2501 337

CATCGCCGTG GTAGCGGCAC æ ATCCCAGCGA TAGGGTCGCT CTGCCTGGTC AAAGGCTTCT TTTCCGAAGA Œ, ပ GACGGACCAG > -1 ပ AAGAACCAGG TCAGCCTGAC AGTCGGACTG E ... S TTCTTGGTCC o z AGAGATGACC TCTCTACTGG H Σ Œ CATCCCGGGA GTAGGGCCCT ഠ 2 တ ACCCTGCCCC TGGGACGGGG Q, H ACAGGTGTAC TGTCCACATG > 2601

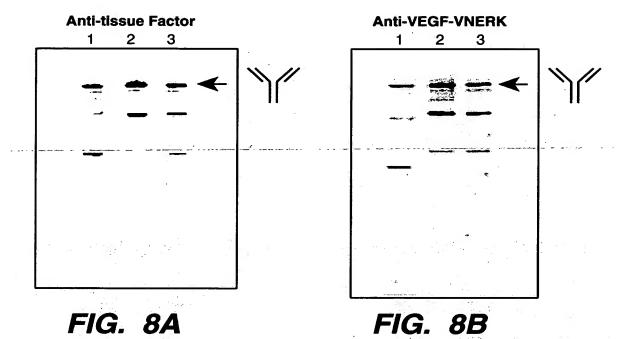
CTCACCGTGG GAGTGGCACC GATGTCGTTC CTACAGCAAG တ >-CCTTCTTCCT GGAAGAAGGA Cz. Cz. CGTGCTGGAC TCCGACGGCT AGGCTGCCGA Ö Ω GCACGACCTG Ω ... > CCACGCCTCC GGTGCGGAGG Ω, AACTACAAGA TTGATGTTCT × GCCGGAGAAC CGCCTCTTG z ω Δ GCAATGGGCA CGTTACCCGT ပ GAGTGGGAGA CTCACCCTCT ω 3 (L) 2701 403

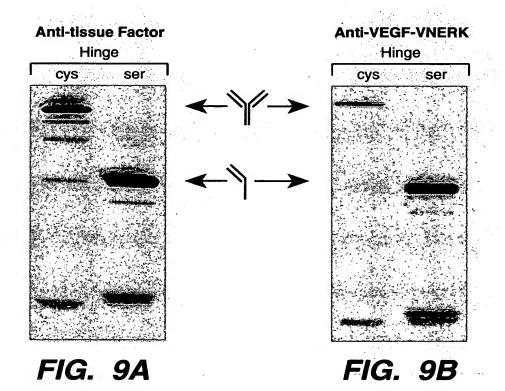
GIGGCAGCAG GGGAACGICT ICTCAIGCIC CGIGAIGCAT GAGGCICIGC ACAACCACIA CACGCAGAAG AGCCICICCC IGICICCGGG ACAGAGGCCC TCGGAGAGGG တ GTGCGTCTTC o TGTTGGTGAT = Z CTCCGAGACG a æ ш GCACTACGTA × Σ > AGAGTACGAG O တ CCCTTGCAGA > z ဇာ CACCGTCGTC O O 3 2801 ACAAGAGCAG TGTTCTCGTC œ S × 437

CTATTCGAAA TAAATAAGCA TGCGACGGCC CTAGAGTCCC TAACGCTCGG TTGCCGCCGG GCGTTTTTTA TTGTTAACTC ATGTTTGACA GCTTATCATC GATAAGCTTT CGAATAGTAG ATTTATTCGT ACGCTGCCGG GATCTCAGGG ATTGCGAGCC AACGGCGGCC CGCAAAAAT AACAATTGAG TACAAACTGT × 2901

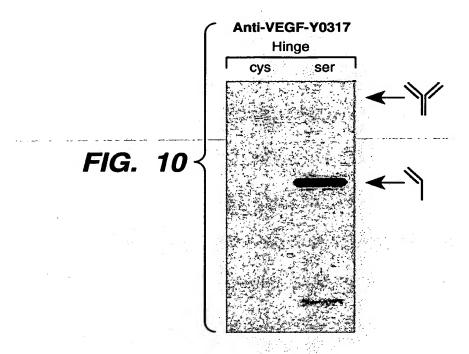
FIG. 7D

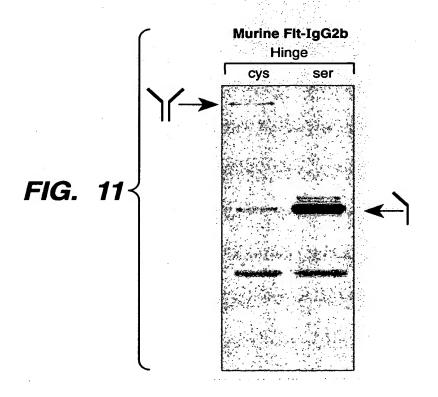
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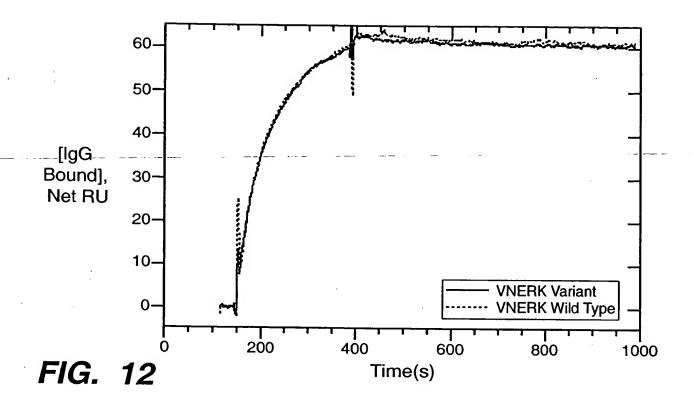


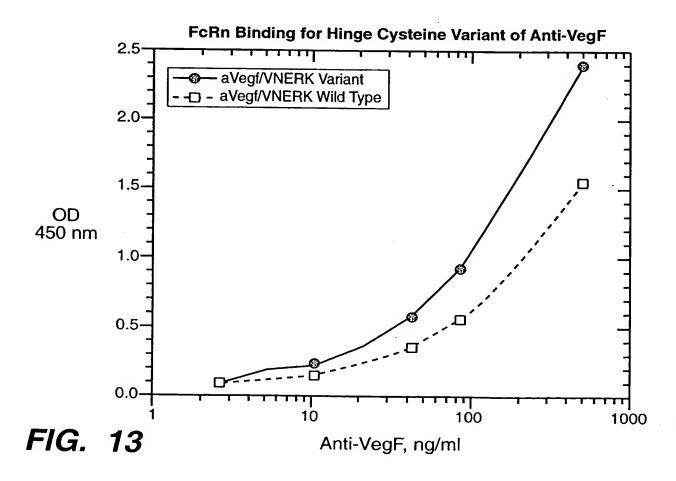
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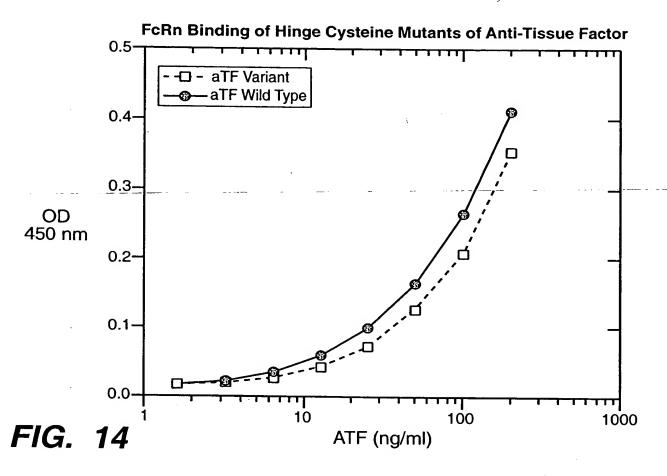


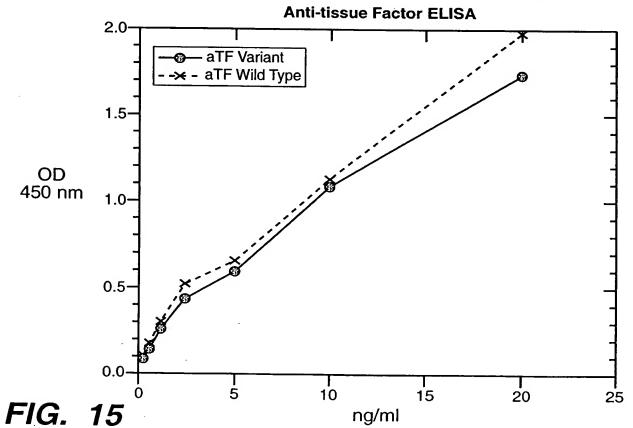
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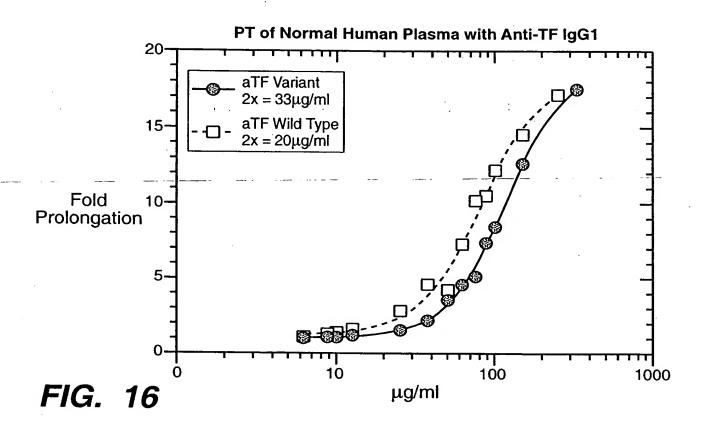




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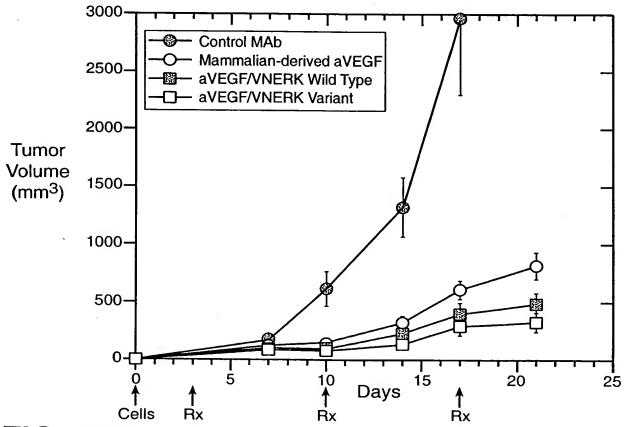


FIG. 17

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